MINERALS IN NUTRITION

By

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REINHOLD PUBLISHING CORPORATION

330 WEST FORTY-SECOND ST., NEW YORK, U. S. A.

1942

Printed in the United States of America by
INTERNATIONAL TEXTBOOK PRESS, SCRANTON, PA.

Letter of Dedication

Dear Davey and Bob:*

Often both of you have shown me the metabolism of your respective fields, railroading and department store management. As a result of our talks, I came to realize the energy exchanges involved in both transportation and consumption of goods. Medicine, too, I thought, deals with these. The study of metabolism in the human body is a study of the train of chemical cause and effect which begins and ends in the various organic depots. It is a study of efficient handling of commodities, this study of the transportation and products of the body.

When I was asked to write a book on Mineral Metabolism for the lay public—a subject not specifically treated as yet in non-technical terminology—there came to my mind a memory of pleasant hours in which we mutually enlightened each other on the intricacies of our various fields. To you then I dedicate this book. I hope it will prove to be to the public for whom it was written (as our talks were to us) a source of illumina-

* David Brown Robertson.
Robert Hays Gries.

tion and new knowledge, widening our common area of insight into the manifold workings of the mineral product, LIFE.

Your friend,

ZOLTON T. WIRTSCHAFTER, M.D.

Cleveland, Ohio
January, 1942.

Note of Acknowledgment

I want to thank my friend, Dr. Harry Hauser, Roentgenologist, Cleveland City Hospital, Assistant Professor of Roentgenology, School of Medicine, Western Reserve University, Cleveland, for the use of the X-ray photographs that are included in this book.

The tables presented in this book were prepared by Miss Helen Mallory and Miss Bessie Wallace of the Dietetic Department of Mt. Sinai Hospital of Cleveland.

I am indebted to my friends, Mr. and Mrs. Paul Hexter and Mrs. Howard Wise, for many valuable suggestions and for aid rendered in the correction of the proof.

ZOLTON T. WIRTSCHAFTER.

Contents

Chapter 1

The Minerals in the Body

What Is a Mineral?

A mineral is a solid or liquid, homogeneous, inorganic, substance which is a direct product of nature. The word *liquid* is used in the definition so as to include water, which is a true mineral, even though we are not used to thinking of it as such. The word *homogeneous* is used because a homogeneous substance is one which has throughout its whole extent essentially *the same chemical and physical properties.*

Besides water, various minerals are present in the human organism. The following chemical elements are found in the body:

Water	Iodine
Sodium	Chlorine
Potassium	Iron
Calcium	Manganese
Magnesium	Cobalt
Phosphorus	Zinc
Sulphur	Bromine
Copper	Fluorine

Our Bodies Are Mostly Water

Living matter contains from 70 to 80 per cent water, and its *vital activity* is inseparably bound up with this high percentage. The organs of different animals, if fats are disregarded, contain almost the same percentage of water; for example, in the muscles of the sheep and ox the percentage is 78; in those of the lobster it is 79; in those of the snail it is 78. Exceptions to this are found only in tissues modified by the storage of food material or for bone formation. Water constitutes over *two-thirds of the body weight* of man.

It was Claude Bernard who stated that all living matter lives in water. In the higher forms of animals and plants we find an internal substance of a liquid nature, called the blood, the sap, or the *lymph;* this forms the "environment" of the cells. Any interference with the amount of water normally present in the body immediately *changes* the activities of the cells.

Rubner measured the amount of water lost by the human body under various conditions of temperature and humidity. Under normal conditions—with the body at rest, and the temperature and humidity as usual—the daily loss amounts to 1.25 per cent of the body weight. In the heat of a warm summer day a man may

lose water at the rate of 4.8 per cent of his body weight, and if he works hard, at the rate of 7.7 per cent. That is, the combination of a hot day and hard work may increase the rate at which water is lost from the body no less than six times the normal. Rubner showed that a loss of 10 per cent of the water content of the body results in serious disorders, and that the loss of only 20 per cent results in *death!* Compare this with the fact that a fasting animal or man can use up almost all its body fat and half of its protein before dying!

Water differs from other foodstuffs in that it is not *stored* in the body if taken in excessive amounts. Of the total water which the body takes up, partly in the form of drink and food, only a very little is removed in the feces. The amount given out by the kidneys varies with that taken in food and drink, and with that lost from the skin and lungs.

Blood is a highly complex fluid in which are suspended spherical bodies—the blood cells. If blood is obtained before it has time to clot, the solids can be separated from the fluid portion. The fluid portion is called the *plasma*, and contains about 90 per cent water. It has been estimated that plasma water makes up about 5 per cent of the body weight, and that the watery medium which surrounds the body tissue cells

and is the means of transporting both food and waste materials makes up another 15 per cent. Since these liquids are found to be present *outside* of the cells themselves, they are referred to as *extracellular* fluids. The total quantity of extracellular fluid is about 20 per cent of the body weight. The fluid that surrounds the tissue cells is called the *intercellular*, or *interstitial* fluid. The fluid *within* the tissue cells of the body constitutes 50 per cent of the body weight and is called the *intracellular* fluid. The volume of this intracellular fluid is maintained by the water formed from the combustion of food materials—proteins, fats and carbohydrates—within the body.

Loss of Water from the Body

Water is lost from the body in the urine, saliva, feces, tears, nasal secretions, sexual secretions, milk secretions, vomiting, and by evaporation from the skin and lungs. Under normal conditions, from 60 to 70 per cent of the water is excreted by the kidneys, from 2 to 6 per cent by the intestine, and from 25 to 30 per cent by the lungs and skin.

Kidneys

The amount of urine excreted has been found to be directly proportional to the intake of fluid

and inversely proportional to the quantity given out by the skin and intestine; in other words, the more one perspires, the less becomes the urine output. Water is required by the kidneys to eliminate certain waste products resulting from the combustion of foods within the organism. If sufficient water is not provided for this purpose, these waste products will accumulate in the body. The amount of solid waste material that must be thrown off by the kidneys is about 35 grams daily. Normal kidneys require at least 500 cc. (over a pint) of water a day to excrete this amount of waste. If the kidneys are diseased, considerably more water will be needed to eliminate the same amount of waste.

Skin and Lungs

At ordinary temperatures, the water content of the air inhaled is extremely small, whereas the air exhaled is almost completely saturated with moisture. Many experiments have shown that, under normal conditions of temperature and humidity, from 800 to 1500 cc. (over a quart) of water is used daily for vaporization from the skin and lungs. The process of vaporization is not much affected by the amount of water available, but uses what it needs to keep

the body temperature normal, even at the expense of the water content of the body.

Intestines

In cases of diarrhea, the amount of water in the feces is increased, and a very large quantity may be lost as a result of this disorder. The feces in man contain from 70 to 80 per cent of water, and in infants from 80 to 85 per cent. The water lost in this way in adults amounts to from 50 to 200 cc. daily, and in infants from 35 to 100 cc.—a rather low percentage of the total amount of water lost each day.

Digestive secretions

Saliva is secreted continuously into the cavity of the mouth by the parotid and other glands located under the mucous membrane, or lining, of the mouth. The secretions of these glands differ somewhat; the secretion of the parotid is the most watery. The sight and smell of food brings about a free flow of the saliva, causing the familiar "mouth watering." The total volume of saliva produced in 24 hours amounts to 1500 cc.—about three pints. The mixed saliva contains about 99 per cent water.

Gastric juice obtained from human beings, when free from bile, is a perfectly colorless, clear

liquid containing 99.4 per cent water. An adult man of average size produces 2500 cc. ($2\frac{1}{2}$ quarts) of gastric secretions in 24 hours. It is interesting to note that stimulation of the nerves that supply the stomach causes a secretion of gastric juice, and that cutting these nerves reduces, but does not abolish the secretion.

Bile is the external secretion of the liver; it is secreted more or less constantly, and is stored and concentrated in the gall bladder. From the gall bladder it is ejected into the intestine, particularly when digestion is going on actively. About 500 cc. (over a pint) of bile is secreted daily, the water content of which is about 97 per cent.

Pancreatic juice is secreted intermittently from a gland called the pancreas, especially when food enters the small intestine. The volume of pancreatic juice produced in 24 hours by an adult has been estimated at 700 cc. This fluid contains over 98 per cent water.

Intestinal juices are secreted in large amounts by the small intestine, and the secretion is slower in the colon, or lower bowel. Between 2000 and 3000 cc. (two to three quarts) of a secretion of 98 per cent water are produced daily in the intestines of an adult.

The *total* volume of digestive secretions pro-

duced each 24 hours by an adult is 8200 cc.—*more than two gallons!* Many patients lose body fluids abnormally by vomiting, diarrhea and drainage from wounds. Circumstances which interfere with the re-absorption of this fluid cause a large and rapid loss of water. This reduction in the volume of body water is known as *dehydration;* and the loss of water is entirely from the *extracellular* fluids, and not from the water *within* the body cells.

What Other Minerals Does the Body Contain?

Besides water the body, as well as its secretions and excretions discussed above, contains the commonest mineral elements on earth: sodium, potassium, calcium, magnesium, chlorine, iodine, phosphorus, sulfur, iron, copper, manganese, zinc and cobalt. It has been shown that a little less than *one per cent* of the weight of protoplasm is composed of minerals. The minerals are not mere inert substances, but take an *active* part in the processes essential to life.

The supply of *energy* that is necessary for all the changes in the body comes from chemical reactions occurring *in solution*. The fluids which permeate and bathe all the cells of the body are solutions containing energy in chemical form. This liquid is utilized by the cells to carry

on their reactions. Depending upon the type of cell, varying reactions are induced in this common medium; different products are formed and different amounts and types of energy are liberated.

In considering foodstuffs, such as proteins, carbohydrates and fats, as sources of body energy we often forget that energy is not the only thing required. In order to use this available energy the integrity of the mechanism for its conversion, that is, *the living cell*, is no less important. For the preservation of this integrity the simple mineral elements are as indispensable as the organic foodstuffs and the vitamins. Numerous investigators have shown that normal physiological activity is not possible in the presence of protein, carbohydrate and fat and water *alone*. These energy-yielding constituents may be present in abundance, and yet the tissues are incapable of performing their functions *unless certain mineral elements are added*.

The pioneer worker in this field was the British physiologist, Sidney Ringer, who first showed the enormous importance of minute amounts of certain minerals in maintaining a normal condition and proper performance of functions in living tissues and cells. Ringer proved that the heart of the frog and turtle, when bathed with physio-

logic salt solution (.85 gram of salt in 100 cc. of water), continued beating for some time. The heart beat, however, gradually grew more and more feeble, until at last it ceased altogether with the heart muscle in a relaxed state. When extremely small quantities of potassium or calcium salts were added to the salt solution the heart beat could be maintained. Ringer also proved that efficient and prolonged contractions of the heart of the frog or turtle could be produced by the following mineral salts in the fluid (sodium chloride 0.90%, calcium chloride 0.025%, potassium chloride 0.03%, sodium bicarbonate 0.003%).

If strips are cut out of the turtle heart and then placed in sugar solution, the heart muscle strips soon cease to beat; but if a small amount of salt (sodium chloride) is added to the sugar solution rhythmic muscle contractions return. When a strip of turtle heart muscle which has been made to cease beating by immersion in sugar solution is placed in a very weak solution of calcium chloride before it is transferred to a sodium chloride solution, spontaneous contractions will return earlier and continue for a longer time. If more than the correct amount of calcium is present in the solution, the beats are found to become smaller and smaller and finally they will

cease altogether. When attempts are made to bathe a turtle heart with blood serum from which the calcium has been removed, the heart soon ceases to beat. The addition of a small amount of calcium to the liquid readily and promptly restores the heart beat.

The mineral element potassium does not appear to be essential for the maintenance of the heart beat. This does not necessarily mean that potassium is an unessential constituent of the liquid, since there is a sufficient store of potassium in the muscle fibers themselves to supply the heart muscle with this mineral element. We do know that potassium has a profound influence on the heart beat, since an increase in potassium in the fluid slows the heart beat and causes a marked relaxation of the heart muscle between the beats. If more potassium is added to the fluid the heart comes to a standstill in a greatly dilated condition.

Investigations of the efficiency of various mineral salt solutions on the hearts of warm-blooded animals have shown that the proportion of the salts must be somewhat different from that used for the frog or turtle (cold-blooded hearts). The most efficient proportions, as might be expected, are those present in the blood serum of the particular animal that is under investigation.

Locke found the following composition most efficient: sodium chloride 0.9%; calcium chloride 0.024%; potassium chloride 0.042%; and sodium bicarbonate 0.01 to 0.03%.

The work begun by Ringer has been continued by many investigators, and has been extended into observations of the effects of *variation* of mineral elements, not only upon maintenance of physiologic activities but also upon rapidity of cell growth, division and reproduction. Loeb made the important discovery that cell division can be begun and carried to an advanced stage of development in the unfertilized eggs of several organisms by varying the composition of the inorganic salts of the medium. These results show the immense importance to the growth and activity of living cells of their inorganic constituents, that is, those which contain no carbon.

Macallum has shown the similarity in composition of sea water and blood. Sea water has been steadily increasing in mineral elements since the geological period when the ancestors of the warm-blooded animals adapted themselves to land life. Today it differs from blood serum in having a higher concentration of magnesium and a lower concentration of potassium; otherwise the mineral composition of the two is the same.

The question now arises as to how these min-

eral elements in solution in our body waters play such an important role in the human economy in health and nutrition? How do they maintain a normal condition and proper performance of the vital functions in our bodies? Why are certain mineral elements vital?

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Chapter 2

The Action and Distribution of Minerals

Pure water is not a good conductor of electricity. If, however, minerals such as common salt are dissolved in water, the resulting solutions are found to be good conductors of electricity. Minerals which produce this change in the conductive properties of water are called *electrolytes*. When dissolved in water such minerals undergo important changes. Some of their molecules *divide* into two or more parts, or, as chemists say, dissociate. These fragments of molecules are called *ions*. Thus sodium chloride (common salt) splits up into sodium ions (Na^+) and chlorine ions (Cl^-). These ions move about freely in the solution, and for this reason were given the name ion, which signifies a wanderer.

Each ion has an electrical charge attached to it, the presence of which is indicated by a small plus or minus sign, depending on whether it is charged positively or negatively. Now it is important to remember that sodium in the form of an ion differs from ordinary metallic sodium.

Davy isolated *metallic sodium* and showed that it *decomposed water*. The electrically charged sodium ion does not. It is thus evident that the electrical charge greatly modifies the usual chemical properties of sodium and similar minerals. In view of the large water content of the human organism, it is not pleasant to contemplate what would happen if metallic sodium were introduced into the body.

As we have just seen, the ions formed by dissociation of any molecule in a solution are of two kinds: one is charged with positive electricity and the other with negative electricity. The sum of all the positive charges is always equal to the sum of all the negative charges. The solution is therefore electrically *neutral*. All protoplasm contains a solution of mineral salts. These salt solutions have certain properties. One of these properties of fundamental importance is that water solutions of the common salts are *good conductors of an electric current*. The British physicist, Michael Faraday, found that when a current flows through a solution of common salt (sodium chloride), the sodium moves down with the current to the negative electrode (cathode). The chlorine moves up against the current to the *positive* electrode (anode). Since the metal part of the salt (sodium) moved down with the

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current, Faraday called such wandering metals *cations*. The word is derived from the Greek *kata*, down and *ion*, going. The negative part of the molecule was called an *anion* (Greek, ana, up). Only particles with charges on them move in an electrical field. If sodium moves down with the current it must be positively charged and the chlorine moving up must be negatively charged. Faraday did not know or explain where the sodium got its charge. He thought that the action of the current separated the neutral sodium chloride molecule into positive and negative particles.

A few metals, such as sodium, potassium and calcium, act rapidly upon water even at ordinary temperatures, liberating one-half of the hydrogen contained in the water. All the oxygen combines with the metal to form compounds which belong to the class known as *bases*. The reaction which takes place when water is decomposed by ordinary sodium may be represented as follows:

$$\text{Sodium} + \text{water} \rightarrow \text{sodium hydroxide} + \text{hydrogen}$$

Ordinary sodium and chlorine molecules cannot be present in the reaction:

$$\text{Sodium chloride} \rightleftarrows \text{sodium} + \text{chlorine}$$

because ordinary sodium decomposes water violently, and chlorine is a gas only slightly

soluble in water and possesses a very disagreeable odor. On the other hand, as we all know, sodium chloride forms an odorless and permanent solution. Therefore the sodium in the above reaction has a positive electrical charge and the chlorine a negative charge; that is, they are *ions*.

Thus we have seen that, when a salt dissolves in water, as it does in living matter, it breaks up into electrically charged particles. Living matter then contains a large number of these electrically charged particles. It is important to note that not all compounds break up, or *dissociate*. Only those compounds dissociate whose solutions are good conductors of electricity. For example, sugar does not break up, and its solution is not a good conductor of electricity. According to the dissociation theory the molecules of sodium chloride break up into the ions of sodium Na^+ (positive charge) and chlorine Cl^- (negative charge). The sodium ions (Na^+) are attracted to the negative pole (cathode); and on coming into contact with the cathode they give up their positive charge and then become *ordinary* sodium atoms. In a similar manner the chlorine ions, on being discharged at the positive pole (anode), may either be given off as chlorine gas or may attack the water. The ions that are attracted to the negative pole are spoken of as *cations*, and

those that are attracted to the positive pole are termed *anions*. Thus sodium, potassium, calcium and magnesium are cations (+). Chlorides, sulfates, phosphates and bicarbonates are anions (—). Since ions are usually more active chemically than molecules, most of the chemical properties of solutions are due to ions rather than to molecules.

Ringer, working before the introduction of the modern ionic theory of solutions, did not express his results in the language of that theory. He did not refer to his results as due to "the effects of molecular concentration of sodium, calcium, potassium or magnesium ion." However, there is no doubt that Ringer appreciated that the results he obtained were due to one ion of the combination of mineral salts that he used. He also recognized the antagonistic action of different ions. Because Ringer's work appears to be in danger of being forgotten, it is important to remember that when the ionization theory had obtained but little credence, he demonstrated the action of sodium, potassium and calcium ions on the heart muscle of the frog and turtle.

As we have seen, the sum of the electropositive elements *equals* the sum of the electronegative elements. The proteins are in the acid, or electronegative, category because proteins

function as anions in the blood plasma. The composition of the blood plasma may be compared with that of 0.9 per cent salt solution. The blood plasma closely resembles other body fluids. Differences in the composition of other fluids are due to the varying protein content.

Blood

Red blood *cells* differ greatly in mineral composition from blood *plasma*. The chief positive ion (cation) of the red blood cells is potassium. The cells and the blood plasma cannot interchange cations, but anions (negative ions) can be exchanged. The potassium content of red blood cells in all species is nearly constant and represents about 420 mg. per 100 cc. The calcium in blood occurs almost entirely in the plasma. Magnesium, unlike calcium, is not confined to the plasma, but it is present in the red blood cells to a greater degree than in the plasma.

Muscle

The muscles of a human being account for 40 per cent of his body weight. The muscle cells are the chief "storehouses" of potassium in the body. Muscle tissue contains very little chloride and what is present has been found to be extracellular. The chloride in muscle is about

one-fifth of that present in blood plasma. Muscle contains a heat-destructible organic compound containing phosphoric acid. Muscle tissue also contains phosphorus in the form of creatine phosphate. Iron is also found in muscle in small quantities. This mineral element helps in the respiratory function of cells.

The muscle cells appear to be impervious not only to sodium but also to chlorides, phosphates, and sulfates. It is well known that lactic acid is formed during muscular contractions. The source of the lactic acid is carbohydrate. The carbohydrates (sugars and starches) are dependent for their physiological action upon phosphorus compounds.

Skeleton

Numerous analyses of bone ash have shown that calcium composes about 50 per cent of this ash. It has been clearly shown that 85 per cent of this calcium appears as calcium phosphate and calcium carbonate. Magnesium constitutes only 0.5 per cent of the ash, and sodium, potassium and chlorine are present in even smaller amounts.

Recent x-ray and chemical analyses have shown that bone probably belongs to the apatite series of minerals. This idea was first presented in 1862 by Hoppe, who believed that inorganic

elements in bone were similar to the mineral known as *apatite*. White apatite is found to occur as small needles in many rocks in nature. Crystals of apatite weighing 550 pounds and 72½ inches in circumference have been found. It is used as a fertilizer and is often referred to as "bone phosphate." It is found in beds in granular limestone. Mineralogists believe that apatite represents the phosphates contained in the organisms which originally deposited the limestone.

Cartilage

Although the total amount of minerals in bone may vary, little if any variation is found in the ratio of the amount of calcium present to the phosphorus. This relationship is expressed as $Ca/P=2.5$. Cartilage has been found to be rich in sodium. The amount of cartilage present decreases with age.

When the human organism is exposed to lead, beryllium, strontium, radium and fluorine these substances can be found in the bones. The skeleton should be considered as the main storage point of calcium, phosphorus, and carbonates and also as the storage point of magnesium, sodium and potassium. Because of the skeleton's ability to store and to release these minerals, this bony system is important in mineral metabolism.

Skin

Studies of the mineral content of the skin show the presence of a considerable amount of sodium and potassium. Only a minimum amount of calcium, magnesium and phosphorus is stored in this organ. That the skin is the normal site of chloride storage has been proved in studies on infants and adults. Chloride (about 30 grams) is present in the adult skin. This amount of chloride constitutes one-third the chloride content of the adult body.

Nerve Tissue

Phosphorus is abundantly present within complicated organic fat structures in nerve tissues (phospholipids). The brain contains more potassium than sodium, and more magnesium is present than calcium. Sulfur, iron and traces of manganese, zinc, copper, bromine and arsenic are found in the "master tissue."

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Chapter 3

What Salt Does in the Body

Sodium occurs chiefly in the extracellular body fluids, that is, in the blood plasma and in the body fluids between the cells. Potassium, on the other hand, occurs chiefly *within* the cells, as in muscle and red blood cells. The intercellular fluids of the skeletal and muscular systems are the chief storage points of sodium. One third of the total body sodium stores is present in the skeleton and another third in the muscles.

With maturity a diminution of intercellular fluid occurs. Since sodium is always found in the extracellular fluid, one would expect a proportional reduction in the amount of sodium and chlorine in the adult as compared to the new born. This has been found to be the case. Sodium and chlorine are the only two elements which decrease proportionately with age.

About one-third of the total chloride content of the body is present in the skin and the tissue under it. Many studies indicate that the skin is the normal location of chloride storage. Sodium is associated with chlorides and with bicarbonate.

As it occurs in the body it composes the largest factor in the "total base," or alkali, of the body.

St. John has clearly shown with rats that life cannot be supported and normal growth cannot take place when the sodium intake is too low. No human diet, even without added salt, contains so little sodium that it cannot support life. The amount consumed in the United States is 4 grams of sodium or 10 grams of sodium chloride (NaCl) per person per day. It is reported that in Europe about twice this amount is consumed. When 35 to 40 grams of sodium chloride are ingested by a normal person, swelling of the body occurs. The tissue of a normal adult contains about 60 grams of sodium. When vegetable intakes are high, sodium chloride is particularly desired. The liberal use of sodium chloride facilitates the formation of digestive juices. It permits a freer flow of saliva, gastric juices, and other intestinal secretions. It is in the medium of the sodium ion and the chlorine ion that the vital actions of digestion take place. The requirement of sodium and chloride cannot be defined separately. They are consumed as salt and excreted together. On very low chloride intake growth is retarded and animals are stunted. If a great deal of sodium chloride is consumed, some of it may be retained in the body, which

results in a swollen condition known as *edema*, even in the normal adult. Hence very high intakes may be harmful.

After being taken into the body, or ingested, chloride is rapidly absorbed from the intestines and deposited temporarily in the skin and the spaces between the cells. It is then excreted in the course of four or five hours. When chloride intake is diminished the urine becomes free from it. When intakes are liberal the kidney eliminates the excess. Although urine is normally the principal means for the removal of sodium and chlorine ions, they are also excreted in the feces and in sweat. When the excretion of these ions in the sweat or feces is large, that in the urine is decreased.

The relation between salt intake and water intake is very important in the way the body utilizes sodium and chloride. With low-salt, high-protein intake, the volume of urine is governed by the excretion of urea, and the usual amount of water is required for urine formation. With low-salt, high-water intake, minerals are swept out and "water intoxication" results. With high-salt, low-water intake the osmotic pressure* of body fluids increases. This condition is called

* The force exerted by substances in solution upon a porous membrane, such as a cell wall, which separates the solution from pure solvent.

"salt fever." As little as 3 grams of sodium chloride per day may produce this condition in infants if water intake is limited. It is certain that in kidney disease the ability to excrete chloride ions is greatly diminished. Large or even normal amounts of sodium chloride in the diet result in the formation of edema. Low-salt diets are used to alleviate this condition; they have even been used in Germany for treatment of skin tuberculosis and other skin infections on the theory that decreased water in the tissues renders them more able to withstand infections. Sodium chloride is the most abundant electrolyte in the blood and intercellular body fluid; in the case of fluids within the cells, potassium and phosphate are the chief ions.

Sodium chloride has two vital functions:

(1) It helps to maintain the acid-base balance of the body; that is, it automatically keeps us "on the alkaline side."

(2) It is largely responsible for the total osmotic pressure* of the extracellular fluids.

Gamble has emphasized that the electrolytes really sustain the blood and intercellular fluids; and while one's attention is frequently drawn to other substances, such as blood sugar, amino acids, lipids and nitrogenous waste products, these are either the nutrient or waste materials

being transported to and from the cells by their real environment of salt solution. Gamble and Ross have pointed out that sodium ions are more important than chloride ions in determining the volume of the extracellular vehicle fluid, since sodium cannot be replaced by any other anion, while chloride *loss* can be replaced by bicarbonate ions formed from carbon dioxide.

The continuous loss of sodium chloride is balanced by a daily intake of from 1 to 2 grams in the food itself and from 2 to 8 grams added in the process of cooking and the vigorous use of the salt shaker at the table. In addition to this amount taken by mouth, from 8 to 10 liters of salt-containing solution made up of gastric juice, bile, pancreatic secretion, and intestinal secretion are poured into the intestinal tract daily.

Body economy is shown by the facts that 95 per cent or more of the sodium chloride is absorbed lower down in the intestinal tract, and that the daily salt loss in the stool is normally less than 0.5 gram a day. Important amounts of sodium chloride are normally excreted by the body in two ways. One is through the sweat glands, the amount lost varying with their activity. Active sweating may produce excretions as high as 2 grams per hour. It has been shown that

the body adapts itself to extreme, dry, heat and that the salt loss in sweat is then much reduced. The kidneys maintain the salt balance by excreting the excess intake; they usually put out from 3 to 8 grams of sodium chloride a day. This is but one example of the kidneys' important function of maintaining a definite concentration of substances in solution in the body fluids and excreting the remainder. Many workers have shown that when no sodium chloride is taken in, or when balance is disturbed by abnormal losses, as in vomiting, diarrhea, etc., the kidneys reduce this excretion to a minimum and conserve salt.

Benedict reported the chloride excretion in the urine of a subject who fasted 31 days and found that 12.3 grams of chloride or 20.3 grams of sodium chloride were put out during that time. Half of this amount was excreted in the first 4 days; during the later days only traces of chloride were found in the urine. One looks for depleted sodium chloride among surgical patients when significant amounts of salt-containing fluid have been lost abnormally from the body by vomiting, diarrhea, drainage from fistulae, profuse wound secretions, and prolonged sweating.

Edema from Too Much Salt Solution

The majority of surgical patients have merely a local wound, with little or no disturbance of the general condition. The sick surgical patient is more critically ill because of temporary malnutrition and body poisoning. These factors often predispose to the retention of water. The administration of distilled water does not produce edema. When the plasma proteins are low the excessive use of salt solution produces edema. When 13 grams of sodium chloride was given per day, edema developed. The edema associated with lack of blood protein, is a sodium chloride edema; the greater the deficiency of the serum proteins, the less sodium chloride it takes to produce edema.

De Wesselow states, "Balance experiments show that approximately a liter of water is retained for every 6 to 7 grams of sodium chloride that accumulate in the body."

Salt *retention* and edema have been found to be associated with pneumonia and other infections. In pneumonia there is retention during the height of the illness and an outpouring of both salt and water with the crisis. A healthy individual can ingest and excrete 35-40 grams of sodium chloride a day. The limit is greatly lowered in sick surgical patients by malnutrition,

sepsis, hemorrhage, draining wounds, severe renal and hepatic disease, long operations, and long anesthesia.

A brilliant technique developed by Lawrence and other workers at the University of California permits, for the first time, the tracing of mineral salts and other materials as they travel through the body. These substances are first given an electrical property, which has been defined "radioactive" and which permits their being identified, as though luminous, when they have later entered the body and traveled to their points of use or deposit.

By means of radioactive sodium Greenberg and his co-workers studied the absorption, excretion and distribution of labeled sodium in rats maintained on normal and low sodium diets. The rate of absorption for sodium is considerably greater than that for potassium. Only about 25% of the sodium was present in the contents and tissues of the stomach and small intestine 10 minutes after ingestion as against an average of 75% for potassium. About 95% of labeled sodium disappeared from the gastro-intestinal tract within an hour. In contrast to the findings on potassium, sodium is not accumulated in the liver, during the period of absorption.

Excretion of Sodium

Rats deprived of sodium excreted less of the equivalent doses than did normal rats, whereas urinary excretion of potassium was found to stay about the same for a period of about three days after administration.

Distribution of Sodium

Tissues and body fluids take up sodium extremely rapidly. Maximum accumulation is reached within 12 minutes. The highest concentration of blood sodium, as would be expected, is found in the blood plasma. The skin, muscle and blood plasma are the most important storage points of sodium.

Body Temperature: Heat Balance

The temperature of the body in health as determined from a thermometer placed in the mouth is around 98.6° F. (37.0° C.). The rectal temperature is about a degree higher and under the arms about a degree lower than the mouth temperature. Some persons have a "normal" body temperature a few tenths of a degree higher or lower than these figures. The temperature of the intestinal organs is higher by 2 or 3 degrees Fahrenheit than that of the skin. The temperature of the liver is about 100° F., whereas that of

the skin when covered with clothes is from 75 to 93° F. The temperature of the bare skin, of course, varies widely with environmental temperature. Strenuous muscular exercise causes a temporary rise in body temperature of from 1 to 4° F.

Heat production is the result of chemical reactions, and is therefore spoken of as the chemical regulation of body temperature. Heat loss depends upon physical factors and hence is called physical regulation. Over 90 per cent of the total heat loss occurs by radiation, convection and by evaporation of water from the lungs and skin. The total quantity of heat lost in 24 hours must of course just equal the amount produced, otherwise the body temperature would rise or fall. Heat production of an average man doing light work is about 3000 calories.

The skin vessels dilate or constrict, and they increase or diminish heat loss automatically by diverting blood from internal regions of the body to the surface or from the surface to the internal organs. A rise in temperature causes an increase in blood volume because the blood is diluted by fluid drawn into the circulation from the tissues. At low temperatures the blood volume is reduced. These changes in blood volume are of paramount importance in the regu-

lation of body temperature. The conduction rate of body heat through the subcutaneous tissues to the skin varies considerably in different persons owing to varying quantities of fat. Fat serves to insulate the body from heat loss. Stout persons therefore become more easily overheated when heat production is increased as in muscular exercise.

The nearer the temperature of the environment approaches that of the blood, the smaller is the amount of heat which can be lost by radiation and convection. By the secretion and evaporation of sweat and the exhalation of water vapor, large quantities of heat are lost from the body. Sweat is a weak solution of sodium chloride in water, with traces of other salts. The percentage of sodium chloride varies between 0.2 and 0.5. Muscular exercise increases the percentage of salt. When the secretion of sweat is very profuse and is continued over a long period, the sodium chloride percentage in the sweat rises markedly. Therefore, if strenuous work is performed for a long period in a high temperature, and large quantities of water are drunk, the body's supplies of chloride are depleted and a deficiency of this ion in the blood and tissues results. Severe cramps occur in the muscles of the legs and abdominal wall (stoker's or miner's cramps). In order to

prevent these effects it is recommended that the thirst be quenched with a weak salt solution instead of pure water.

Addison's disease is the result of lack of function of the interrenal gland (adrenal cortex). Addison's disease is characterized by the presence of muscular weakness, low blood pressure, gastro-intestinal disturbances, pigmentation of the skin and often by the existence of nervous symptoms. Perhaps the most important disturbance resulting from an insufficiency of the adrenal cortex is the decrease of sodium in the blood plasma and the increase of potassium. The decrease in the plasma sodium is accompanied by a corresponding drop in the chloride. It is well known that the reduced percentage of sodium is associated with an increase in the excretion of this mineral salt and water by the kidneys. The presence of defective sodium metabolism, along with adrenal cortical insufficiency, has been clearly established. The administration of sodium salts and water may correct this condition.

It is now generally agreed that there is a loss of sodium from the body in the presence of untreated adrenal cortical insufficiencies in both man and animals. Many workers have shown that extracts of the adrenal cortex help the body to retain sodium in the presence of adrenal cortical

insufficiencies. A patient with mild adrenal insufficiencies can be maintained in moderately good health by the oral administration of salt and water as the sole method of treatment. Sudden deaths due to salt restriction have occurred in patients with Addison's disease and the use of a salt free diet is a hazardous procedure.

The occurrence of a generalized swelling, or edema, associated with menstruation has been reported by many observers. Injections of large doses of sex hormones in dogs result in a striking retention of sodium chloride and water. Women often gain 2 to 3 pounds or more during the week immediately preceding menstruation. Less frequently a transient gain in weight can be noted at or about the expected time of ovulation. The premenstrual gain in weight is associated with the retention of sodium, chloride and water. The increased urinary excretion which follows the onset of menstruation is associated with increased excretion of sodium, chloride and water. The excretion of the female sex hormones in the urine can be correlated with the cyclical changes in the sodium, chloride and water excretion.

Sources

The best food sources * of sodium chloride are as follows:

Foods	*Milligrams Salt per 100 grams of food*	*Remarks*
Caviar	2997	15 gm. serving 349 mg.
Rye krisp	2900	18 gm. (3 pieces) 522 mg.
Butter	2000	10 gram sq. = 200 mg.
Clams, long	1940	
Full cream cheese	1668	30 gm. = 500 mg.
Clams, soft	1500	
American cheese	1452	Average serving about 50 gm. = 726 mg.
Roast beef, canned	1382	
Rye bread	1691	Slice 27-36 gm. or 564
Boston brown bread	1002	3 small slices
Oysters	974	
Graham crackers	873	2 crackers (15 gm.) 131
Whole wheat bread	582	Slice approximately 194
White bread	523	Slice approximately 174
Molasses	523	
Condensed milk	462	
Dates	376	
White fish	295	
Turnip greens	277	
Escarol	276	
Banana	206	
Fresh Coconut	198	

* The tables presented in this book were prepared by Miss Helen Mallory and Miss Bessie Wallace of the Dietetic Department of Mt. Sinai Hospital of Cleveland. Much of the material in these tables was com-

piled from Bridge's "Food and Beverage Analysis," "Art and Science of Nutrition" by Hawley and Carden, and from "Chemistry of Food and Nutrition" by H. C. Sherman.

Note that, when deciding which foods are "high" in a given mineral, it is well to consider the quantity of food which constitutes a normal serving and what cooking does to the amount of mineral. For instance, dried lima beans contain 7 milligrams of iron per 100 grams of beans, as high a concentration of iron as is found in many meats. After lima beans are cooked, only one-third to one-half of the iron content remains.

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Chapter 4

Potassium

Potassium is essential to life. It is widely distributed in both plants and animals. The potassium requirements for normal growth and maintenance have been found to be amply supplied by the potassium content of a diet that is adequate in other respects. So potassium intake need be of no practical concern, because the potassium content of the average diet (2-3 grams per day) is ample to meet the body's needs for this mineral.

Potassium is present within all the cells of every tissue and only a small amount is present in the body fluids. When new body tissues are being built the potassium requirements are at the maximum. Potassium after ingestion is readily absorbed from the intestine, disappears quickly into the tissues, and can be rapidly excreted by the kidneys. The rapid disappearance from the blood stream indicates storage in the tissues such as the red blood cells and the cells of the muscle. Increase in potassium lessens excitability of muscles; stronger stimuli are then needed to cause contraction.

Potassium occurs in the body chiefly in the form of phosphates, chlorides and bicarbonates. The body contains more potassium than sodium, and during periods of growth this difference is even more marked. It is for this reason that it is desirable during periods of rapid growth to supply the body with an excess of potassium over sodium in the food. Milk contains 2.5 times as much potassium as it does sodium. The potassium requirements of adults are less than those of infants and children. Adults require more sodium chloride, and usually consume 1.5 times as much sodium as potassium.

The concentration of sodium in human blood plasma averages 335 mg. per 100 cc.; this is eighteen times the concentration of potassium, which averages 19 mg. per 100 cc. However, potassium predominates in tissue cells. Thus the ratio of the potassium content of the red blood corpuscles in comparison to that of blood plasma is 34 to 1. In muscle tissue potassium predominates, and muscle contains from 3 to 4 times as much potassium as sodium.

In the cell, potassium is associated with phosphorus. Not all the potassium occurs in the ionized state–some of it is in the ordinary form (without an electrical charge). Some potassium is said to be "bound" to complex phosphates.

POTASSIUM

The content of ionized potassium in the blood plasma has been found to be nearly constant, and intake of large amounts of potassium does not increase it. Potassium salts are almost completely absorbed from the gastro-intestinal tract. Less than 10 per cent of the potassium consumed in food is eliminated in the feces, and about 90 per cent of the excreted potassium is found in the urine.

Recently favorable responses to doses of potassium chloride in conditions commonly considered to be allergic have been reported. This led to the presentation of a new concept of allergy, namely, that allergy results from a faulty metabolism of mineral salts.

Because the body does not have the capacity for storing potassium in the intercellular fluid, potassium salts are used to increase excretion of urine; however, persons afflicted with heart or kidney trouble cannot tolerate potassium salts. When there is difficulty in the excretion of sodium and chloride ions, there is also difficulty in the excretion of potassium ion.

An increase in the concentration of potassium accompanies the decrease in plasma sodium concentration and the loss of water in cases of insufficient adrenal secretion. Many investigators have demonstrated the abnormal susceptibility to

small amounts of potassium salts in animals whose adrenal glands have been removed. Many clinical reports indicate the danger of taking in large amounts of potassium salts by patients suffering from adrenal insufficiency.

The effects of withholding potassium from the diet of rats has been the subject of numerous investigations. It was found that the potassium deficiency resulted in the failure of the animals to continue growth, and that death followed. Recently it has been shown that the muscles of animals deprived of potassium take up sodium instead of potassium. In potassium-depleted animals we have a condition in which sodium must occur in the intracellular fluid. In cases of experimental muscular weakness, a decrease in the potassium content of the muscles has been proved.

Sources

The best food sources of potassium are:

Foods	*Milligrams Potassium per 100 grams of food*	*Remarks*
Lima beans, dry	1730	
Meat	1690	
Fish	1670	
Olives	1530	25 gm. average
Molasses	1350	
Dried beans	1200	

POTASSIUM

Foods	*Milligrams Potassium per 100 grams of food*	*Remarks*
Prunes, dried	1030	
Figs, dried	960	
Peas, dried	910	
Lentils	880	
Currants, dried	870	
Raisins	820	
Almonds	740	Average serving 30-50 gm.
Peanuts	650	
Filberts	620	
Coconut, dried	600	
Avocado	570	
Chestnuts	560	
Spinach	540	
Parsnips	520	
Dates	510	
Barley	480	
Whole-wheat cereals	470	Average serving based on 20 gm. dry
Dandelion	460	
Potato	460	

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Chapter 5

Calcium

Calcium is one of the most important of the biological mineral elements. The metabolism of calcium is a slow process and a relatively long time is required for changes to take place. Calcium is present in the body in a larger amount than any other mineral element; it occurs almost entirely in the bones, which constitute the normal storage points, very little being present in the other tissues. However, the small fraction of calcium that is *not* present in the bony tissues is of tremendous importance in determining the state of health of the body.

Calcium occurs in bones in the proportion of three molecules of tricalcium phosphate to one molecule of calcium carbonate; this proportion persists regardless of whether calcium is being deposited in or withdrawn from the bone. Eighty-five per cent of the mineral matter of the bones is composed of calcium phosphate, and it has been estimated that seventy-five per cent of the ash of the entire body is composed of this substance. The normal daily intake of calcium

is approximately one gram. Although this amount of calcium may be taken into the body, it is by no means sure to be assimilated and used. Frequently a large proportion of the calcium occurs in the diet in an insoluble form, and assimilation by the gastro-intestinal tract is impossible. A normal individual maintained on a diet that is poor or deficient in calcium develops a negative calcium balance, or in other words he excretes more than he eats. Sherman believes that to maintain calcium equilibrium the adult diet should contain one gram of calcium for every 100 grams of protein. The existence of an incorrect proportion between calcium and phosphorus intake is frequently as harmful as an absolute lack of either. Calcium should be to phosphorus in the ratio of 1 to 1.5 or 1 to 2. Excessive phosphorus in the diet will reduce the amount of calcium which it is possible to absorb by forming insoluble compounds with the calcium of the diet.

Those portions of ingested calcium and phosphorus which are not assimilated are excreted in the feces. To this excretion of unassimilated calcium must be added that portion of calcium which is thrown out from the blood stream into the urine and feces. It has been estimated that 80-90 per cent of the excretion is by way of the feces and 10-20 per cent by way of the urine.

CALCIUM

Blood Calcium

Nearly the entire calcium content of the blood is found to be present in the serum, where it occurs normally in a concentration of 10 mgs. per 100 cc. The serum contains about three times as much calcium as can be held in an inorganic solution of this type. Authorities are in agreement that calcium in the serum exists in two different and distinct types.

(1) The diffusible type is that portion of serum calcium which can pass through an artificially prepared membrane.

(2) The non-diffusible type of serum calcium cannot pass through the membrane because it is combined with the albumin of the serum.

About 50-60 per cent of the blood serum calcium is of the *diffusible* type. It is this diffusible portion which contains the *active* calcium, which is in the ionized state. The human fluids that are poor in proteins all contain calcium in the ionized form.

Recent studies in calcium metabolism are in agreement that the largest amount of retained calcium is found in the skeleton; however, significant amounts were found in the skin and in the teeth. The retention of calcium in the teeth is as great as in the skeleton. This finding indicates that calcium of certain parts of the teeth is

as mobile as that of the skeleton. The retention in the gastro-intestinal tract, heart and lungs is about the same as that in the skin, and is extremely low in other tissues.

Calcium is absorbed by the body in the small intestine. It is well known that calcium salts are soluble in acid solutions and relatively insoluble in alkaline solutions. Hence, during and after eating, when the stomach has produced an abundance of hydrochloric acid in the gastric juice, ingested calcium will be very soluble and will be present in the ionized state.

When the food and the ionized calcium leave the stomach and come into contact with the alkaline secretions of the pancreas, bile and intestinal secretions the calcium is precipitated. The fatty acids present in the small intestine now can also react with the calcium to form insoluble products. Calcium absorption is greatly retarded by eating excess fat, with the consequent formation of these insoluble calcium products. An increase in the alkalinity of the intestinal juices will decrease calcium absorption.

Lactose (milk sugar) administration increases lactic acid fermentation in the intestinal tract and hence produces an acid medium throughout the intestines. It is for this reason that lactose feeding is advocated for increasing the amount of cal-

cium absorbed. Some workers report that increased calcium absorption can be readily obtained by giving a few drops of dilute hydrochloric acid.

It has been shown that vitamin D promotes a greater absorption of calcium from the intestinal tract, together with an increased absorption of phosphate.

The Functions of Calcium

Bones. The importance of calcium to normal hardening of the bones (calcification) is obvious. Minerals, and in particular calcium, are readily moved in and out of bones. The bones store or yield calcium and phosphate according to the immediate needs of the body. Bones are not inert masses of calcium salts, but contain vein-like passages. Some authorities believe that the presence of an enzyme called *phosphatase* causes the precipitation of calcium phosphate in the bones. Others state that calcium is deposited first in combination with tissue protein and that this complex structure gradually decomposes and is then free to combine with more calcium. None of the theories advanced appears to be adequate to explain the mechanism of calcification at present.

It has been pointed out that the presence of

certain mineral salts of sodium, potassium and calcium in balanced proportions are necessary for vital functions. Ringer showed in the case of the frog's heart that a certain balance must be maintained between various inorganic mineral salts. Sodium chloride alone could not maintain the activity. It was necessary to have present both potassium ions and sodium ions in certain balanced proportions. The alternate waves of contractions and relaxations which are characteristic of the rhythmical action of the heart muscle are related in some manner to interactions of the ions of sodium, potassium and calcium in the living muscle. Calcium appears to be involved in the transformation of chemical energy into muscular contractions. Calcium ions are also necessary for normal coagulation of the blood.

Rickets

Many workers have produced experimental rickets in animals. The cure of rickets with vitamin D, and the effect of ultraviolet light on rickets have all contributed to make us "vitamin D-conscious." Rickets occurs in early childhood, usually from the sixth to the eighteenth month. The defect is due to lack of exposure to sunlight or to a deficiency of vitamin D in the diet. The condition is recognized by enlargements of the

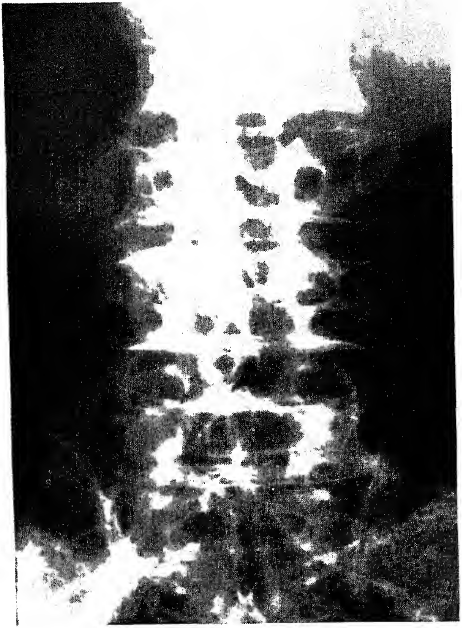

Figure 1A. A front view of the lower spine of an adult showing a marked degree of demineralization of all the vertebrae as compared with Figure 1B.

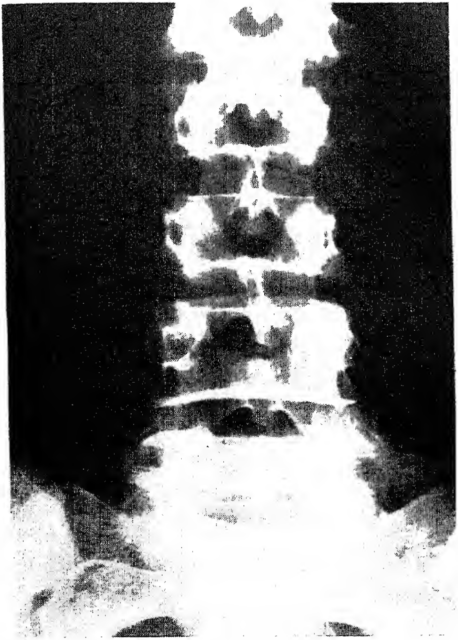

Figure 1B. Front view of the lower spine showing normal mineralization.

wrists, knees and ankles. Closer investigation may reveal that the head is somewhat square and that areas of softness may be present. Teething may be delayed as well as the ability to sit or stand. Moderate enlargement of the cartilaginous portion of the ribs is present.

The muscular system is poorly developed and the muscles are flabby. Naturally all these signs will not be present in every case. In a well developed case of rickets the head has become square and perhaps slightly enlarged. The chest is deformed and shows two lateral rows of enlargements at the cartilaginous portion of the ribs; the abdomen is large and protuberant; the legs are bowed and the posture shows that the ligaments are lax. X-ray examination shows characteristic involvement of the bones, and the phosphorus of the blood is reduced to a marked degree.

The significant changes which take place in the bones in rickets are the relative increase in water content and the decrease in calcium and phosphorus content. It has been demonstrated that rickets is associated with an insufficient retention of calcium, the loss occurring particularly by way of the intestinal tract. Our attention in the past was focussed on calcium, and the importance of phosphorus was overlooked. Experi-

mental investigations have shown that rickets can be produced by diets deficient in phosphorus.

A disturbing factor in the appraisal of calcium metabolism is the inability to determine the amount which has been absorbed, because calcium is not only absorbed but also excreted in the intestinal tract. Calcium in the feces represents not only unabsorbed calcium but also that which has been absorbed and re-excreted in the intestinal tract.

Any substance that prevents the adequate retention of calcium and phosphorus should lead to rickets. An excess of other metals which form insoluble phosphates causes rickets. Instances of rickets due to beryllium, magnesium, iron, lead and tellurium have been reported. Vitamin D prevents or cures rickets by restoring the calcium and phosphorus of the blood serum to the normal concentration.

The amount of calcium and phosphorus in the feces is reduced. How vitamin D heals rickets is as yet not known. Recently it has been shown that it permits a greater absorption of calcium from the intestinal tract, which in turn increases the absorption of phosphorus. The withdrawal of these minerals from the bones is arrested and the stream of calcium and phosphorus from the blood to the bones is restored.

Figure 2A. Side view of an adult spine showing, beside the marked degree of demineralization, compression of the vertebral bodies.

Figure 2B. Normal side view of an adult without compression, with normal mineralization.

Bone Softening (Osteomalacia)

In general this disease usually commences about puberty or in early adult life. The fact that it occurs almost entirely among women is evidence that faulty diet is not alone responsible for this condition. However, there can be no doubt as to the influence of pregnancy and lactation. The distinctive symptom of morbid bone softening (osteomalacia) is pain. The pain, the sensory disturbances, and the difficulty in walking all increase as pregnancy advances. This condition is characterized by softening and distortion of the bony structures, particularly of the pelvis.

It has been found that the most constant factor in bone softening is a net loss of calcium, and hence this disease must be regarded as characterized by a deficiency of calcium in the blood. It has also been shown that new bone laid down during the process of the disease is poor in calcium and richer in organic matter and magnesium phosphate.

Renal Rickets

Renal rickets is a disease of childhood in which chronic kidney disease is associated with bone changes resembling late rickets. The child is usually stunted and deformed. The factor respon-

sible for the bone changes is a deficiency of calcium and phosphorus in the blood. It has been shown that this lack of balance is not due to mineral deprivation or to a lack of vitamin D in the diet. In kidney disease the excretion of phosphorus into the intestines is increased. An increase of phosphorus in the intestinal tract results in a lowering of the blood calcium, due to the formation of insoluble calcium phosphates. No amount of vitamin D will enable it to be absorbed. The result of this condition will be a removal of calcium from the bones.

Parathyroid Glands

The parathyroid glands are situated close to the thyroid glands. The number of parathyroids is usually stated to be four; however, the number and the position of these glands are very inconstant in man. Although the parathyroid glands were first described in 1880 their function was not recognized at that time. Removal of these glands results in a marked calcium reduction of the blood serum from normal levels and a rise in the phosphorus level. Rapid, noisy breathing, high temperature, increase in the heart rate, frothing of the mouth, and twitchings of the muscles, followed by muscular contractions, occur from 48-72 hours after the removal of

these glands. The spasm of the muscles of the larynx and chest lead to death from asphyxia. The above described condition is called *tetany*.

Low serum calcium values are also found in tetany produced by other means than parathyroid deficiency. The tetany that accompanies rickets and bone softening also indicates that calcium deficiency is the direct cause of the increased muscular excitability. The concentration of ionized calcium is the determining factor in the production of tetany. The calcium ion tends to depress the nerve and muscular excitability caused by the potassium and sodium ions in the tissue fluids. The tetanic symptoms can be rapidly abolished by the injection of calcium salts in the ionic state. The injection of extracts derived from the parathyroids will also relieve this condition.

The extracts of the parathyroid gland, when injected into animals whose parathyroids have been removed, have been shown to be able to maintain the calcium of the blood serum at the normal level. However, when the calcium has been raised to the normal level and doses of the extract are continued at frequent intervals, overdosage occurs. This is evidenced by the fact that serum calcium values are now found to be 2 to 3 times higher than normal, together with loss of

appetite, depression, weakness, frequency of urination, vomiting and diarrhea. This continued overdosage may lead to death. The excess calcium in the serum following the administration of the parathyroid extract has been shown to be derived from the calcium stores of the skeleton.

In man, an increase in the parathyroid secretion results in hardening of various organs. This is caused by increase of the calcium content of these organs. It has been reported in the heart, lungs, arteries, thyroid, kidneys, spleen, skin and eyes. The bone changes are secondary to the removal of calcium brought about by mobilization of calcium from this storehouse as a result of the oversecretion of one or more of the parathyroid glands. The bones become softened and weakened. The long bones may bow or break and the vertebrae may even collapse.

Sources

The best food sources of calcium are:

Foods	*Milligrams Calcium per 100 grams of food*	*Remarks*
Cheese: Swiss	1086	Usual serving 50-60 gm.
Cheddar	990	
American	930	
Full Cream	635	Serving 30-50 gm.
Nuts (Filberts)	287	Serving probably 30 gm.

CALCIUM

Foods	*Milligrams Calcium per 100 grams of food*	*Remarks*
Evaporated milk	276	
Molasses	258	
Almonds	230	
Kale	197	
Milk	120	Average 200 cc. (1 glass =240)
Navy beans, dried	158	
Pablum (average serving after cooked)	156	Based on 20 gm. dry cereal
Ice cream	150	
Kidney beans, dried	132	
Egg yolks	130	Approximately 4 yolks
Cottage cheese	82	
Eggs, whole	68	2 Large
Navy beans, cooked	50	For comparison
Kidney beans, cooked	39	For comparison

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Chapter 6

Magnesium

Knowledge of the importance of magnesium in nutrition has lagged far behind that of the other inorganic elements that are present in the body to any considerable extent. In 1932 it was conclusively demonstrated that magnesium is a nutritional essential. Magnesium is present in the body cells in a far greater concentration than is calcium. Magnesium and calcium are both stored in the bones. The concentration of calcium in the plasma is four times greater than that of magnesium.

The amount of magnesium taken in varies with the type of food. The chief source of magnesium in the average diet is vegetables. It is in the chlorophyll, or green coloring matter, of vegetables that we find magnesium present. Since for this reason an adequate amount of magnesium is present in the human diet, the problem of specific deficiency in magnesium does not arise normally. The average intake of magnesium in this country is 0.27 gram per day, and it appears to be sufficient. However, diets consisting of re-

fined cereals and generous amounts of milk, advocated for children of the pre-school period, may contain less than the ideal amounts. In the process of refining, much of the magnesium is removed from the grain, and milk contains comparatively little of it.

The absorption of magnesium from the gastrointestinal tract in most respects resembles the absorption of calcium. Magnesium is excreted in the feces and in the urine. Fifty to eighty per cent is excreted by the intestinal tract, and the remainder by the kidneys. When solutions of magnesium are injected into the veins, ninety per cent is excreted in the urine. The ingestion of acid causes a shift in the excretion of magnesium and calcium from the feces to the urine. The absorption of magnesium from the intestine is diminished by excessively high intake of fats, calcium and alkalies. The retention of magnesium is proportional to the immediate need of the body. Infants and growing children have large retentions of magnesium; it is necessary to maintain the normal structure of growing new tissue.

Magnesium is found in both the red corpuscles and serum, but the concentration of magnesium in the red cells is greater than in the serum. About eighty per cent of the magnesium in the serum is diffusible. Unlike calcium, magnesium

is present in large amounts in the red cells, most of it being in the form of magnesium ions. The red blood cells contain 5.4-7.8 mgs. of magnesium per 100 cc., and the blood serum 2.5 mgs. of magnesium per 100 cc. The magnesium content of serum has been found to be decreased during menstruation, pregnancy and in rickets.

The largest amount of magnesium is found in the bones in the form of magnesium phosphate and magnesium carbonate. A great deal more calcium is present in the bones than magnesium—about 100 to 200 times as much. Chemical analyses of various tissues show that magnesium is present in the muscles and in other tissues in a concentration of about three times that of calcium. The effects of calcium and magnesium are usually antagonistic.

Too little magnesium in the diet of animals produces profound changes. Within a few days after the animals are placed on a diet low in magnesium, dilatation of the blood vessels (the presence of an increased amount of blood) and a state of over-excitability may be observed. The above findings are followed by nutritional failure and kidney damage. After the onset of over-excitability, until death of the animals, growth ceases and nutritive failure becomes apparent. Other symptoms of malnutrition, such as general

loss of hair, a rough and sticky coat, diarrhea and finally edema appear.

Studies of magnesium deprivation have revealed that there are two distinct phases to this deficiency. The first phase is manifested by the dilatation of the blood vessels (vaso-dilatation) and over-excitability. The second phase is characterized by the development of malnutrition and kidney damage. During the first phase the concentration of magnesium in the plasma drops sharply and then rises to a peak shortly after the onset of over-excitability. During the second phase, the concentration of magnesium in plasma falls at a slower rate and does not reach values lower than 1.0 mg. per cent of plasma-magnesium. The magnesium content of the red corpuscles is reduced to about one-half the normal value. Little retardation of growth occurs during the first phase, but marked reduction in growth occurs during the second phase.

The condition of over-excitability induced by magnesium deprivation was first observed by McCollum and his co-workers. This state of over-excitability represents a new form of tetany, distinguished by a normal blood calcium and a marked reduction in the magnesium blood plasma value. In animals, a pronounced protrusion of the eye-balls frequently appears several

days before a convulsion. This has been described as being a symptom of a combined magnesium and calcium deficiency.

Many investigators have found that animals placed on a low magnesium diet developed marked changes in the kidneys. When the magnesium deficiency is continued, the kidneys become progressively damaged. An increase in the calcium content of the kidneys is present in animals fed a magnesium-deficient diet. It appears that calcification plays an important part in the degeneration of the kidneys. Solutions that are low in magnesium content appear to favor calcification. The calcification that occurs in the kidneys can partially be explained by this effect.

Anesthesia can be induced by magnesium injection. If calcium is given to such an anesthetized animal, it causes an awakening which in turn is followed by a lapse to the original anesthetic state. Sedative and hypnotic effects can be obtained by controlling the magnesium concentration of the serum.

Recent work has clearly shown that magnesium excretion in man does not parallel calcium elimination. Thus in exopthalmic goiter, it has been found that magnesium may be stored in spite of an enormous calcium loss. No condition of excessive magnesium excretion has as yet been

reported to have occurred in man. It will be interesting to see what future research into hypertension and other pathological conditions may develop along the lines of the effect of magnesium deficiency. Magnesium is an important mineral element, as evidenced by its high concentration in the body cells.

Sources

The best food sources of magnesium are:

Foods	*Milligrams Magnesium per 100 grams of food*	*Remarks*
Wheat germ	511	1 tablespoon to 3 oz. used daily
Honey	386	
Endive	380	Usual portion 25 grams
Kohlrabi	370	
Fresh figs	303	
Chocolate	293	
Almonds	251	
Cowpeas	208	
Dried lima beans	188	
Peanuts	180	
Dried beans	156	
Pecans	152	
Dried peas	149	Fresh 38
Hazel nuts	140	
Dried kidney beans	139	
Walnuts	134	

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Chapter 7

Phosphorus

Phosphorus is essential for vital activity and particularly for cell division. The amount of phosphorus in the body has been found to vary from about 14 grams at birth to approximately 670 grams in the adult. The distribution of the body phosphorus reveals that 70-80 per cent is present in the skeleton, 10 per cent in the muscles, and 1 per cent in the nervous system. Since phosphorus is an essential component of every cell, the remaining fraction is widely distributed. Phosphorus is present in all cell nuclei in the form of phosphoric acid molecules which, together with other constituents, form nucleic acid.

The requirement of the growing animal for phosphorus is relatively high. The minimum requirement for the adult man averages about 0.88 gram of phosphorus per day, merely to replace the loss of this mineral element from the body. It has been estimated that only a few of the American dietaries fall below this level. In the case of the adult, there is less danger of phos-

phorus deficiency than of calcium deficiency.

Many workers have observed that even a moderate reduction of phosphorus in the diet limited the possibilities for growth. Animals placed on diets deficient in phosphorus may thrive for a short period, presumably until exhaustion of the available phosphorus stored in the skeleton. Later, however, there follows growth failure in the young, and loss of body weight, weakness and collapse in the adult animal.

Phosphorus deficiency occurs more frequently in cattle than in other species. In dairy cows the deficiency causes failure and depravement of appetite, stiffness and muscular weakness. The failure of nutrition is clearly evidenced by loss in weight, and good recovery is noted when phosphates are added to the diet. Cattle may develop an intense craving for phosphorus which manifests itself in bone eating, particularly in regions where the soil is deficient in this element.

The forms of phosphorus ingested depend upon the type of food that is consumed. Milk contains a protein called *casein,* which is relatively high in phosphorus. A small amount of phosphorus is excreted into the gastro-intestinal tract, and that which is found in the stools is derived from unabsorbed food. This fecal phosphorus has been found to be chiefly in the form

of calcium phosphate and magnesium phosphate. Excessive dietary phosphorus, by forming insoluble compounds with the calcium of the diet, will reduce the amount of calcium that it is possible to absorb. Local conditions within the intestinal tract may prevent the assimilation of phosphorus and calcium. In the presence of large amounts of free fatty acids, soluble calcium and magnesium compounds are made insoluble. High-fat diets, or any condition in which fat absorption is impaired, increase the absorption of phosphorus, because the calcium which would normally combine with the phosphorus has been utilized in the formation of calcium "soaps." (Any product of a reaction between a fat and an alkaline substance is a "soap" in chemical parlance.)

About 70 per cent of the phosphorus is excreted by the kidneys, and 90 per cent of this amount is in the form of inorganic phosphorus. Diets low in phosphorus, high in calcium, and low in fat produce a urine that is almost free of phosphorus.

The minerals found in bone are calcium, phosphorus, magnesium and small quantities of sodium, chlorine, fluorine and iron. In bone, calcium exists in the form of calcium carbonate ($CaCO_3$) and also as tricalcium phosphate,

$Ca_3(PO_4)_2$. Many workers believe that the calcium carbonate and calcium phosphate of bone are not present as separate compounds, but as complex compounds. Phosphorus constitutes 16 per cent of the ash of bone, while calcium constitutes 36 per cent and magnesium 0.5 per cent. The phosphorus present in the skeleton in the form of tricalcium phosphate represents the largest storage of phosphorus in the body. The ratio of the amount of calcium to phosphorus as evidenced in bone ash is 36% : 16%. The concentration of phosphorus present in bone ash is a little less than one-half the concentration of calcium.

Recent work has demonstrated the importance of phosphorus in the muscular mechanism of man. One-tenth of the total body phosphorus is found in the muscular system. Here the phosphorus is in the form of phosphoric acid, and is in various complex combinations with organic compounds. During muscular contractions this compound breaks down, liberating phosphoric acid. Although our knowledge of the chemical reactions which occur during muscular contraction and recovery is not complete, *phosphorus compounds are essential for normal muscle activity*.

That phosphorus is present in brain and nerve

tissues has long been known. The phosphorus exists in this situation as a constituent part of the fat, and fats that contain phosphorus are termed phospholipids. It has been suggested that the phospholipid content of a tissue is an index of the tissue's activity. In rapidly growing malignant tumors, the phospholipid concentration is higher than in normal tissue. When one considers the extent and the variety of the functions of the brain, it is not surprising to find the presence of phosphorus in the fat present in this master tissue.

The quantity of organic phosphorus present in the blood is much greater than that of inorganic phosphorus. The concentration of the inorganic phosphorus of the blood changes during life. Thus, in infants it is 5 mg. per 100 cc. of serum, and in adults it is 3-4 mgs. per 100 cc. of serum. Phosphorus is present in a much greater concentration in the cells than in the serum. The inorganic phosphate of the blood serum is present in a completely ionized state and not in complex combinations with other minerals.

A close relationship exists in the animal body between the metabolism of sugar and that of phosphorus. The ingestion of sugar causes an immediate decrease in the excretion of phosphorus, and this is later followed by an increase

in the excretion of phosphorus to above the normal level. The inorganic phosphate of the blood appears to be intimately related to metabolism of glucose, a form of sugar. It is probable that the formation of hexose phosphate (glucose phosphate compound) is an essential step in the process of utilization of glucose. The rate of intestinal absorption of glucose is increased in the presence of phosphate.

It has been shown that vitamin D, in the form of cod liver oil or Viosterol, permits a greater absorption of phosphorus and calcium from the intestinal tract. When excessive doses or amounts of vitamin D are ingested, the serum phosphate concentration and the concentration of calcium may be greatly increased. Both of these effects are more likely to occur in normal individuals than in children who have rickets.

Many observations suggest a relationship between the action of excessive dosage of vitamin D and the parathyroid glands, because, after the removal of these glands from monkeys, vitamin D is not able to cause an increase in the calcium and phosphorus level. Both vitamin D and extract of the parathyroid gland cause an increase in the concentration of phosphorus and calcium in the blood. Both cause the withdrawal of cal-

Figure 3A. X-ray of wrist of 5½-month-old infant with rickets. Note cupping and flaring of lower ends of forearm bones and lack of development of wrist bones.

Figure 3B. X-ray of 5½-month-old normal infant. Development is normal. Forearm bones and wrist bones show normal development. Compare density of these normal bones with Figure 3A.

cium from the bones and increase the excretion of calcium and phosphorus in the urine.

This overdosage of vitamin D gives rise to calcification (hardening) of various organs and bony changes. Stones are formed in the kidneys and various types of kidney damage are often induced. Calcification of the heart, lungs, arteries, thyroid, skin and eyes have been reported. On the other hand, the bones become softened and weakened.

After leaving the stomach, food requires about four to six hours to traverse the small intestine, during which time active absorption of nutrient materials takes place. Diarrhea may lead to large losses of minerals; in cases of severe diarrhea, this loss of minerals may become excessive. At the same time an increase in the amount of fat lost in the feces becomes evident. If fat is not utilized and fatty acids are excreted by the intestine, they form insoluble calcium "soaps," and thus cause a lowered calcium and phosphorus retention. Increased intestinal activity may increase the fecal output of calcium and phosphorus to twice that of the normal. The so-called "fatty" diarrhea is frequently accompanied by removal of minerals from the bones. The decrease in phosphorus and calcium concentration in the serum is due to

defective absorption and increase in the loss of minerals in the feces.

In the chemical processes associated with rickets, the importance of phosphorus as well as of calcium is significant. A marked increase in the excretion of phosphorus and calcium is present, and as rickets develops the excretion of phosphorus and calcium increases to even higher levels. The excretion of phosphorus, however, exceeds that of calcium. Under normal conditions the amount of calcium in the stools is always greater than the amount of phosphorus, because calcium is "bound" not only to phosphorus, but also to fatty acids. In rickets, the amount of phosphorus in the stools frequently exceeds that of calcium.

We are at present unable to determine the amount of phosphorus which has been absorbed because phosphorus is not only absorbed, but also excreted into the intestinal tract. The phosphorus in the feces represents, then, both unabsorbed phosphorus and that which has been reabsorbed and re-excreted into the intestinal tract. Determinations of inorganic phosphorus in the blood and investigations in which rickets has been produced by diets deficient in phosphorus have shown the importance of this mineral in rickets. Other metals, such as beryllium, magnesium,

iron, lead, and tellurium have been reported to cause rickets. In such cases the rickets is due to an excess of the metal, which forms insoluble phosphates and hence leads to rickets.

The administration of vitamin D results in restoring the phosphorus and calcium of the blood to normal concentrations. The amount of calcium and phosphorus in the feces is reduced. Vitamin D has recently been shown to cause a greater absorption of calcium from the intestinal tract, which in turn increases the absorption of phosphorus. Hence, the withdrawal of these minerals from the bones is arrested and the stream of calcium and phosphorus from the blood to the bones is restored.

Sources

The best food sources of phosphorus are:

Foods	*Milligrams Phosphorus per 100 grams of food*	*Remarks*
Cheese: Swiss	812	Average portion 50-60 grams
American	701	
Cheddar	682	
Sweet chocolate	400	
Nuts	333-480	Not usually used in 100 gram amounts
Turkey	373-423	
Roast veal	287	

Foods	*Milligrams Phosphorus per 100 grams of food*	*Remarks*
Canned fish	245-276	
Chicken	208-270	
Ham, fresh	269	
Cottage cheese	262	
Whole egg	224	2 large
Beef	220	
Liver	205-220	
Lamb	202-212	
Cooked navy beans	200	
Mead's cereal (approx. 100 gm. cooked)	140	20 gm. dry
Baby Ralstons	120	20 gm. dry

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Chapter 8

Sulfur

Sulfur occupied a prominent place among the few elements known to the ancients, and played an important role in the older views concerning the composition of matter. Sulfur occurs in nature both pure and combined with other substances. In certain volcanic regions, especially in Sicily, large deposits of so-called "free" sulfur are found, and in the United States large deposits occur in Louisiana. Large quantities of sulfur also occur in nature in the form of compounds known as *sulfides* and *sulfates*. These are called "inorganic," as they do not contain carbon. Since sulfur is a constituent of protein, it is present quite generally in vegetable and animal matter. Plants probably can form proteins from the inorganic sulfates, but animals cannot. Small amounts of inorganic sulfate are found in the blood and tissues of animals. Unlike phosphorus, organic sulfur compounds (those containing carbon) are essential for the maintenance of life, and every cell contains sulfur.

If a diet containing a limited amount of casein

(one of the proteins of milk), or some other protein, is fed to animals, growth is curtailed. But if to the diet is added a supplement of the sulfur containing amino acid, *cystine*, growth is resumed. This discovery that the sulfur-containing amino acid is needed for growth, has been confirmed many times. In experiments on the Queensland Downs, the wool clip of lambs was greatly increased by supplementing the protein-deficient pasturage with blood meal, a protein material of high cystine content. The conclusion that cystine is an essential factor appeared to be established until a second sulfur-containing amino acid, *methionine*, was discovered. This, as well as cystine, will stimulate growth of animals. Recently reported experiments with diets containing mixtures of pure amino acids show that methionine is indispensable, and that cystine and methionine represent the most important sources of sulfur in metabolism.

Proteins are the most widely distributed of the organic compounds that contain sulfur. The *nitrogen* content of various types of protein is relatively constant and has been found to be 16 per cent; but the sulfur content of proteins varies greatly. This is illustrated by casein (milk), which contains 0.80 per cent sulfur, gelatin 0.20 per cent, wheat 1.03 per cent, corn 0.60 per cent,

lactalbumin (milk) 1.73 per cent. Wool contains 3.55 per cent, and human hair, especially red hair, contains over 5 per cent of sulfur. Although there are marked differences in the sulfur content of the various proteins, the ratio of nitrogen to sulfur in the various proteins is approximately 16:1.

Methionine is almost completely absent from protein derived from skin sources, such as wool and hair. The sulfur present in the above proteins is in the form of cystine. Active muscular tissue has a high content of methionine. The protein of milk, casein, has a relatively high content of methionine and a low content of cystine. In lactalbumin, the other important protein of milk, the cystine and methionine content are nearly equal.

Vitamin B_1, or thiamine, is one of the biologically important sulfur-containing compounds. Another is insulin. In highly purified crystalline insulin, cystine has been isolated as the sulfur constituent.

Thiocyanates are another type of sulfur compounds; these are found in the saliva and other body fluids. The liver is probably the place where the thiocyanates are formed. Poisonous cyanides are thus converted into the relatively harmless thiocyanates by this method. The saliva

of smokers contains a greater concentration of thiocyanates than that of non-smokers. Some workers believe that thiocyanates are synthesized by the salivary glands and that the presence of thiocyanates is due to the absorption of the salivary thiocyanates through the gastro-intestinal tract.

That the body conserves and re-utilizes some of the sulfur-containing amino acids is well known. It has been estimated that 30 per cent of the cystine produced in the body from the breakdown of protein is again utilized in the liver for the formation of a sulfur-containing bile salt called *taurine.* Methionine and cystine, however, cannot be replaced by taurine in nutrition for meeting growth requirements.

The pigments that normally give color to the hair and to the skin, and even the marked discoloration that occurs in conditions like Addison's Disease, and in certain tumors, contain sulfur. In the brain and nervous tissues, compounds of sulfur with fats are found, which are called sulfatides. Little is as yet known concerning the physiology of these compounds.

Since most of the sulfur content of our food occurs as methionine or cystine in the proteins that we consume, the amount of inorganic sulfate in the diet is relatively small. The normal range

of the sulfur present in this inorganic sulfate of human blood serum has been reported as 0.8-1.7 mg. per cent. In kidney disease the sulfate concentration of the blood is increased. The inability of diseased kidneys to concentrate urine parallels the increase of the sulfate concentration of the blood serum. Some workers believe that a retention of the sulfate is an earlier indication of kidney impairment than is afforded by other symptoms.

When an individual is on an ordinary diet that contains about 14-16 grams of nitrogen, about 80 per cent of the total sulfur of the urine is in the form of inorganic sulfate. This inorganic sulfate is formed and excreted in the urine when sulfur is completely oxidized in the body. The remainder of the sulfur content of the urine is in various organic combinations. The amount of sulfur excreted daily depends upon the sulfur intake, which in turn depends upon the amount of protein that is eaten or metabolized. Sulfur enters the body chiefly in the unoxidized form of protein sulfur. The inorganic sulfate excreted in the urine amounts to nearly 1 gram of sulfur per day. On a high-protein diet both the total sulfur and the inorganic sulfate excretion are increased.

When the protein intake is adequate, sulfur intake is not a nutritional problem. The body

excretes nitrogen and sulfur in constant proportions during periods of health, and determinations of this proportion may be used as a measure of protein metabolism. The recognition of methionine as an "essential" protein unit of widespread occurrence has resulted in a renewed study of sulfur compounds and their importance in human economy.

There exist many conflicting opinions concerning the use of sulfur in the treatment of various pathological conditions. Recent work clearly shows that there is no evidence that colloidal sulfur or inorganic sulfate introduced into the body in any way can be used for the synthesis of the sulfur-containing amino acids. The injection of sulfur in man caused an increase in the sulfur excretions by amounts much greater than the amount injected. The injection of sulfur thus caused or tended to create a sulfur *deficiency*. Only the sulfur-containing amino acids can be utilized by man as a source of sulfur.

Sources

The best food sources of sulfur are:

Foods	*Milligrams Sulfur per 100 grams of food*	*Remarks*
Wheat germ	325	Used 1 tablespoonful to 2 or 3 oz. daily

Foods	*Milligrams Sulfur per 100 grams of food*	*Remarks*
Lentils	277	
Cheese	263	
Cowpeas	240	
Lean beef (20% protein)	230	
Kidney beans	227	Fresh 56
Peanuts	224	
Clams, round	224	
Dried peas	219	
Egg white	216	
Clams, soft	213	
Dried peaches	212	
Dried coconut	203	
Boston brown bread	201	3 small slices
Hazel nuts	198	
Eggs	195	
Brussels sprouts	194	
Cabbage greens	173	

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Chapter 9

Iron

Nearly fifty years have passed since Macallum stated, "The discovery of micro-chemical methods for detecting iron in cells has aided me in establishing the generalization that the most important of all elements in the life of every cell is an iron-holding compound." Now, all workers are in agreement that iron is an essential constituent of plant and animal protoplasm. Although the amount of iron present in man is small, it is of vital importance in the living processes concerned with the *transport of oxygen* and with the *metabolism of food materials* within the cells.

The most important organic form of iron is *hemoglobin*, the pigment of the red blood corpuscles. The iron content of hemoglobin is nearly the same for all species of animals, amounting to about 0.33 per cent. Hemoglobin combines with oxygen to form oxyhemoglobin, a compound which readily gives up its oxygen when exposed to an environment of low oxygen tension. A liter of blood plasma can take up only about 3 cc. of oxygen, and 1,000 cc. of oxygen is nec-

essary for tissue needs. If man had to depend for his oxygen requirement upon the solubility of oxygen in the plasma alone, his circulatory system would have to contain about 300 quarts of fluid, which is about four times his normal body weight! Due to the efficiency of hemoglobin, our oxygen needs are amply handled by only 6 quarts of blood. It is to hemoglobin that we owe our activity.

In man the quantity of hemoglobin appears to be regulated by the demand for oxygen and its supply. At high altitudes where the amount of oxygen is decreased, the quantity of hemoglobin in the blood is increased. Barcroft studied the blood of the natives in the Cerro de Pasco region of the Peruvian Andes, which are 14,000 to 15,000 feet above sea level. His findings clearly show that the quantity of hemoglobin was greatly increased in the natives that were studied in comparison to the normal amount observed in persons at sea level.

In all the tissues of both plants and animals, an iron-containing compound called *heme* is present. Heme is very widely distributed in nature, and its chemical composition is the same no matter where it is found. The presence of these heme compounds has been proved wherever metabolic change takes place, and their function

is probably that of a promoter of chemical reactions. Hemoglobin is a *protein* compound in which the *iron* complex is a heme. The hemoglobin of various species differs only in the protein portion, since the heme complex has the same composition in all forms of life. Hemoglobin is found in blood and in muscle. Cytochrome and hematin are other iron compounds which are found in the tissues and cells of the body.

Hemoglobin is the chief iron compound of the body, and two-thirds of the total iron of the adult is present in this form. However, iron exists in many combinations in the body other than in the red cell hemoglobin. The most important of these are in muscle hemoglobin, liver, spleen and marrow tissue. Iron has been recognized, even in the blood, in forms other than hemoglobin. Recently a non-hemoglobin iron that differs from hemoglobin iron has been demonstrated in the red cells. Blood iron itself consists of several entities, and chemical methods alone give but little information concerning these various iron components. Hence, the metabolism of iron in the body, which at first appeared to be simple to follow, becomes complex because in nearly all tissues, iron may be present in *two or more different forms*.

It has been estimated that the amount of iron in the body at birth is 0.4 gram and in the adult, 4.5 grams. Various workers have estimated different amounts of iron as being necessary for meeting normal adult requirements. The amounts advocated have varied from 5 to 15 mg. per day.

Metabolism of Iron

Some mineral elements differ between themselves in the number of atoms of other elements which they are able to hold in combination. Water is a combination in which one atom of oxygen combines with two of hydrogen. The number which expresses this combining ratio between atoms is a definite property of each element and is called *valence*. Iron differs from many metals in that it is able to form *two* series of compounds in which iron has two different valences. Those compounds in which the iron has a valence of two are known as *ferrous* compounds, while those in which it has a valence of three are known as *ferric* compounds.

Absorption of iron compounds from the stomach has as yet not been proved. Primarily, the absorption of iron occurs in the small intestine in the form of the ferrous iron (valence of two). Ferric iron compounds, with a valence of three, are changed in the gastro-intestinal tract

to the ferrous state. Some workers believe that the hydrochloric acid of the gastric juice makes for greater solubility of the iron in the food, and aids in ionization of the iron. A lack of hydrochloric acid hence may interfere with the absorption of the iron present in food. Recent work suggests that under the conditions of acidity or alkalinity present in the gastro-intestinal tract, it is the ease with which the ferrous salts are ionized that is the important factor in determining the relative rate of iron absorption. When food is eaten just before or immediately after the ingestion of iron salts, there is frequently observed a smaller rise in the serum iron than during conditions of fasting.

When ingested iron reaches the stomach, the free hydrochloric acid that is normally present ionizes and dissolves the iron not already present in solution, and delays the formation of insoluble and un-ionizable iron compounds. When the iron reaches the upper portion of the small intestine, it is subjected both to the influence of the alkaline intestinal juices and to certain agents which remove oxygen from it. These agents change any three-valent iron to the ferrous or two-valent state, and the iron is absorbed from the intestinal tract as ferrous iron.

When iron is absorbed, it passes directly into

the blood plasma. The plasma iron is composed not only of the iron absorbed from the gastro-intestinal tract, but also of the iron that is derived from the breakdown of hemoglobin and other iron compounds of the body cells. Since about 90 mg. of iron are broken down daily, and the amount in our food rarely exceeds 15 mg. per day, the iron derived from the normal break-down of metabolic activities is of great importance. When the body reserves of iron are ample, very little is assimilated. When there is a need for iron, a much larger quantity will be absorbed from the gastro-intestinal tract into the blood stream. It appears that the body is capable of assimilating or rejecting iron according to its need for this element, and that the lining of the small intestine is the tissue responsible for its acceptance or rejection.

By means of radioactive iron it has been possible to trace the fate of this marked iron and to differentiate the iron found in tissues, bones or fluids from that coming from body storage points and from the destruction of red cells. It was found that the plasma is the medium of transporting iron from the intestinal tract to the points at which it is utilized. Absorption from a given dose of iron in animals is complete at the end of 18 hours. At the end of 18 hours the radioactive

iron is in the large intestine and no absorption is further demonstrable. Within a few hours after feeding, radioactive iron finds its way into the red cells. The plasma transports iron from the gastro-intestinal tract to the red bone marrow to be made into hemoglobin, and to the liver and spleen for storage. Small amounts of iron are found in the urine; the source of this iron is the inorganic iron of the blood plasma. The amount of iron excreted by the gastro-intestinal tract varies with the amount in food and the body needs for this element.

Anemia

When the level of the hemoglobin concentration in blood is below 10 grams per 100 cc. of blood, an anemic condition is considered to exist. The type of anemia that is benefited by iron treatment contains less than the normal amount of hemoglobin per cell, and the red cells are smaller than normal. This type of anemia is observed among infants maintained on a milk diet. It has been demonstrated that rats soon develop nutritional anemia when fed an exclusive diet of whole milk. This anemia can be prevented by the addition of inorganic iron, since whole milk is relatively low in iron. Although copper does not appear to be essential to the absorption or storage

of iron, it was shown to be essential to utilization of iron to build hemoglobin. Copper increases the ability of the human infant to utilize stored iron. Observations show that in the first six months of life, when rapid hemoglobin formation takes place, the iron stores of the body are thoroughly utilized. In this period of early infancy, which is characterized by high copper and iron stores, copper depletion parallels iron depletion. The addition of copper, wherever iron treatment is indicated, appears useful. Other deficiencies than that of copper may prevent the utilization of iron in the food, and the general nutritive state cannot be overemphasized.

The anemia of pregnancy is a condition characterized by decrease below normal levels for the period of gestation in red blood cells or hemoglobin, or both. Most of the anemias of pregnancy appear to fall into the iron-deficiency group, and yet normal gestation places no great demand upon maternal iron stores. It has been estimated that the total additional iron requirement for this period amounts to approximately the amount contained in 500 cc. of blood. A recent study reports that in over 50 per cent of clinic patients a true anemia of pregnancy was present. Such anemias result from either a deficiency or impaired utilization of iron. Not

infrequently a combined type of anemia was present, caused by a need for both iron and protein.

There are many observations on the possible relationship between rickets and anemia. Some workers have shown that anemia in rickets is due to factors such as poor nutrition, and not directly to injury of the bone marrow. Children fed good diets, but low in vitamin D, developed rickets without anemia. The administration of vitamin D to infants suffering from anemia and rickets did not raise the hemoglobin level. The administration of iron salts to ricketic infants did cause an increase in the hemoglobin content to a satisfactory level.

It has been proved that inorganic iron is absorbable and is of value in nutrition, and that organic iron compounds are of no value. The body cannot utilize even the iron in blood when it is ingested, because the iron is so firmly bound in an organic form. Small quantities of iron are supplied by everything that we eat, but no single food contains enough iron to provide an adequate intake in a single portion.

Sources

The best food sources for iron are:

Foods	*Milligrams Iron per 100 grams of food*	*Remarks*
Beef (liver)	8.30	
Molasses	7.97	
Sweetbreads	7.50	
Pancreas	6.00	
Egg yolk	7.60	About 4 yolks
Beef kidney	5.50	
Calves' liver	5.40	
Beef heart	4.80	
Raisins	4-6.90	No figure for cooked fruit; cooking might decrease amt.
Corned beef	4.10	
Beef (round steak)	4.10	
Roast veal	3.60	
Beet greens	3.55	
Oysters	3.14	
Mushrooms	3.14	
Beets	2.98	
Shrimp	2.69	
Eggs	2.52	2 large
Other meats	2.50	or less

Listed as good sources by some, but require consideration of loss in cooking:

Navy beans	8.25	Cooked 2.05
Dried lima beans	7.00	Fresh or canned 2.16-2.22
Dried peas	5.70	Fresh 1.77
Apricots, dried	6.74	Cooked, dried 2.01
Prunes, dried	3.80	Stewed, dried 0.81; canned 1.53
Spinach, raw	4.00	Canned, strained 1-2.2
Nuts	2.14-6.84	Consider quantity to be used

IRON

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Chapter 10

Iodine

Iodine occurs in traces in all the rocks, soils, waters and dusts of the earth. During the disintegration of igneous rocks, iodine is liberated, and its occurrence in soils is due to these rocks. Iodine is held more firmly by very fine than by coarse, sandy soils, and is thus washed from the sandy soils into the sea. The iodine in sea water is absorbed and concentrated by *seaweed*. The regions which have very little iodine are those which were once covered by glaciers, such as the Great Lakes Region; and it is no coincidence that these regions are not only low in iodine, but are the regions in which *goiter* is most prevalent. On the other hand, wherever iodine is abundant, goiter is rare. In Japan, where seaweed is a common ingredient of the diet and where the iodine intake is therefore probably greater than that of any other people, goiter is practically nonexistent.

In man, the thyroid gland is a two-lobed reddish-yellow organ that weighs about 20-25 grams and is situated at the sides of the larynx and

windpipe. In 1895, Baumann made the important discovery that the thyroid gland contained iodine in a firm organic combination. Later, it was found that the colloid material of the thyroid gland was the protein, *globulin*. The active principle of the thyroid glands was isolated by Kendall. From 3 tons of fresh thyroid glands he obtained 33 grams of a substance, named thyroxine, which had the same pharmacological properties as whole thyroid gland.

Because it has been impossible to detect thyroxine in the blood and lymph leaving the thyroid, and because thyroglobulin has been demonstrated in the above-mentioned fluids, it has been concluded that free thyroxine is not secreted by the thyroid gland, but that thyroglobulin is secreted by this organ. Other iodine-containing compounds have also been isolated from the thyroid gland. The iodine content of thyroxine accounts for only one-fourth of the total iodine of the thyroid gland of adults. The iodine content of this organ appears to vary and increases with age. In the new-born infant the iodine content of the gland has been found to be less than 0.1 mg., and in the adult up to 15 mg. The total iodine content of the body has been estimated to be 20 mg., of which about one-half is present in the thyroid.

IODINE

How Iodine is used in the Body

Although we are accustomed to thinking of iodine in terms of a poison or as a disinfectant, it is essential in minute amounts. Iodine is probably absorbed from the gastro-intestinal tract, regardless of the form in which it is eaten. Not all the iodine that is ingested as food or drink is absorbed. Iodine compounds are secreted into the saliva, sweat, tears, milk and bile secretions. When iodine is taken by mouth, it appears in the urine in a few minutes. Even on an almost iodine-free diet, a daily excretion of iodine has been reported. When iodine is lacking in the diet, the body holds on to its iodine with great care, and hence only small quantities of it are required for replacement and growth.

The thyroid gland is the principal storehouse for iodine, and iodine and thyroid function are inseparably related. The utilization of iodine to form thyroid hormone is an important part of thyroid activity. It has been shown that the thyroid gland has the ability to abstract iodine from the blood stream, and that iodine is constantly present in human blood. The iodine is contained principally in the colloid substance. The normal blood iodine averages about 4.5 micrograms per cent, and increased blood iodine values are reported in cases of over-active thyroid. In this

condition there appears to be an increase in its mobilization, circulation, and excretion. It is evident that a profound disturbance of iodine balance exists when the thyroid is too active.

Iodine is a normal constituent in the urine; and the excretion of this element fluctuates with the food intake and other factors. The normal person excretes about 50 micrograms daily of iodine. The iodine that appears in the urine is not in the form of thyroxine, but as a simpler compound. In cases of goiter, about three times the normal amount of iodine is present in the urine.

Thyroid Secretion

Many experiments upon various species have established the fact that the secretion of the thyroid is necessary for normal growth and development and for maintaining the normal level of metabolism. Sir William Gull, in 1874, connected atrophy of the thyroid with loss of hair, thickening and dryness of the skin, and loss of mental and physical vigor. This condition was later designated as *myxedema*, because it was thought that the thickening of the tissues beneath the skin was due to mucin. It was later discovered that in Gull's disease (myxedema) the heat production was greatly lowered. This fall in heat production was found to be the character-

istic effect of removal of the thyroid gland in both man and animals; and this lowering of metabolism leads to stunted physical, mental and sexual development.

The effects of thyroid removal in lambs, rabbits, goats or calves causes retarded skeletal growth together with arrest of sexual development. Other effects of thyroid removal in the young are delay in bone-formation, poor growth of hair, subnormal intelligence, lack of vigor, thickening of skin, and reduction in basal metabolism. The administration of thyroid extract (thyroxine) corrects the effects caused by thyroid removal.

Gudernatch, in 1914, removed the thyroids from tadpoles, keeping a definite number of the same hatch as controls. The thyroidless tadpoles grew larger but did not become frogs, while the controls developed into frogs within the normal time. When small amounts of thyroid substance were fed the tadpoles, there was a rapid loss of weight, and the change took place in from four to five days. Complete change of form for the normal larvae requires 104 days; thyroid feeding caused this time to be shortened to 20 days. Other forms of iodine produce similar effects, but not to the degree that thyroxine does.

Many observers have noted in dogs that feed-

ing fresh meats causes an enlargement of the thyroid gland, and that feeding sea fish increases the iodine store and reduces the size of the gland. Marine and Lenhart showed that pig's liver was the most potent of a large variety of meats in causing an enlargement in the thyroid of both dogs and cats. Recent work also suggests that the calcium, magnesium and phosphorus ratios in some manner influence thyroid function. These findings are considered evidence of a decreased activity of the thyroid gland.

Cretinism (thyroid deficiency in infants) is most common in the valleys of the Alps, Pyrenees, Himalayas and other regions where goiter is prevalent, and is the final result of thyroid failure. However, in other regions some cases of cretinism appear in infants who do not have goiter. The condition is then believed to be due either to congenital absence of the gland, to atrophy of thyroid before or after birth, or to destruction by infection. A cretin is a dwarf. An absence of the thyroid secretion in infancy or early childhood is responsible for this condition of retarded and abnormal growth, arrested sexual development, mental deficiency, coarse facial features, dry skin, enlarged tongue, faulty bone formation and decrease in heat production.

Myxedema occurs in adults or older children

Figure 4A. X-ray of 16-year-old wrists of a female Cretin showing a bone age of $9\frac{1}{2}$ years. Note undeveloped, small, centers of ossification in the wrist as compared with normal Figure 4B.

Figure 4B. X-ray of wrist of 16-year-old normal girl showing complete development and maturation of wrist bones.

and corresponds to the cretinism of infants. This condition follows atrophy and destruction of the thyroid. Infrequently it results from an operation in which too much of the thyroid gland has been removed. The puffy appearance of the skin, and the dry, brittle and sparse hair are indicative of this disorder. It is also characterized by lethargy, increase in body weight, and sluggish mentality.

Simple goiter, myxedema and cretinism are believed to be different stages of the same nutritional fault, and are primarily due to thyroid failure. Animals living in the sea are free from this condition. Marine and Lenhart concluded that goiter is a deficiency disease due to an insufficient supply of iodine. They were able to demonstrate that iodine added to the water supply of large colonies of brook trout entirely prevented the development of goiter.

Kimball, in 1917, conducted a large-scale experiment in goiter prevention in the school population of Akron, Ohio. He gave 2 grams of sodium iodide in 0.2-gram doses distributed over a period of two weeks each spring and autumn. Physical examination of the pupils revealed the same striking preventive and curative effects that had been observed in animals. Human goiter was found to be preventable by iodine. The general-

ization made from the work with fish, birds, sheep and pigs was applicable to man.

Iodine is effective in the prevention of goiter when given in any form and by any means. Sea salt which contains iodine was the first means of administration. Now artificially iodized salt has, to a great extent, replaced the other means of practical prevention. The daily amounts of iodine required for prevention of goiter obviously vary in different localities, ages, climates and diets. The normal requirements of the body for iodine are not yet known, but it has been estimated that from 0.04 to 0.08 mg. would suffice for the normal daily needs of an adult.

Sources

The best food sources of iodine are:

Sea foods	*Non-goitrous region*	*Authority*
	Parts per billion of dry matter	
Cod liver oil	3000-13000	U. S. Bureau of Fisheries
Cod liver	7670	U. S. Bureau of Fisheries
Codfish	5350	U. S. Bureau of Fisheries
Oysters	1800-3500	U. S. Bureau of Fisheries
Salmon	570-2200	U. S. Bureau of Fisheries
Flounder	1480	U. S. Bureau of Fisheries
Crabmeat	1460	U. S. Bureau of Fisheries
Red Snapper	1440	U. S. Bureau of Fisheries
Conch	1140	U. S. Bureau of Fisheries
Shrimp	1100	U. S. Bureau of Fisheries

IODINE

Foods	Goitrous region	Non-goitrous region	Authority
	Parts per billion of dry matter		
Wheat	1–6	4–9	McClendon
Oats	10	23–175	McClendon
Carrots	2	170	McClendon
Carrots	..	507	Okla. Agr. Expt. Sta.
Lettuce	..	618	Okla. Agr. Expt. Sta.
Potatoes	85	226	McClendon
Potatoes	..	10–216	Frear
Potatoes	..	90–700	Ga. Agr. Expt. Sta.
Cabbage	..	776	Adolph & Whang
Cranberries	..	26–35	Morse
Asparagus	..	946	Okla. Agr. Expt. Sta.
Radishes	..	946	Okla. Agr. Expt. Sta.
Tomatoes	..	379	Okla. Agr. Expt. Sta.
Milk	265–322	572	Remington & Supplee
Butter	140	..	McClendon

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Chapter 11

Other Minerals

Aluminum

Most investigations help to substantiate the generally accepted conclusion that aluminum is found in all plants and animals. The human diet contains aluminum both in the foods themselves and from cooking utensils. It appears that no knowledge is as yet available to determine whether it is an essential element for the tissues, although many investigators report the presence of aluminum in the tissues in varying quantities. In a study of the possible role of aluminum compounds in animal growth and nutrition, no difference in growth and reproduction of rats fed an aluminum-free diet or one containing 0.6% of aluminum chloride was reported. However, the addition of large amounts of aluminum *salts* to the diet produces severe rickets, due to the fact that phosphate assimilation is retarded. In large amounts, the aluminum interferes with the absorption of phosphorus and tends to cause low phosphate values in the blood serum.

The scientific work relating to the assimilation

of aluminum by the human organism has failed to give satisfactory results. The chief reason for this is that the quantities of aluminum absorbed are very small, frequently less than one part in a million parts of blood, and the purest reagents obtainable for making the search can rarely be secured quite free from this element. By means of the modern quartz spectograph, it has been demonstrated that normal blood contains no aluminum except in traces. Although some workers have reported that the American diet contains over 3.0 grams of aluminum per week, mostly from cooking utensils, it is practically all excreted in the feces under normal conditions, and is therefore not at all harmful.

The part played by aluminum in nutrition still remains unexplained.

Arsenic

Arsenic is sometimes one of the most common poisons and at others it is one of the most useful drugs. The assumptions that arsenic plays a part, as does iodine, in the functioning of certain tissues, or that its presence is merely due to ingestion of traces of this element in the food, are debatable. Examination of the blood, urine, hair and milk has led to the opinion that arsenic is found "normally" in a large number of per-

sons, depending upon the character of their food, drink and environment. Recent work indicates that arsenic may play some part in physiological processes. During menstruation the arsenic content of the blood was found to be increased by 50 per cent, and in pregnancy it rises to a maximum during the fifth and sixth months.

An interesting observation has been made that the arsenic in shrimp is only slightly stored in the bodies of rats, whereas inorganic arsenic fed to these animals accumulates to a marked degree. It is held from the above observation that arsenic in shrimp is in a complex combination. Ingested arsenic is excreted by the gastro-intestinal tract and urine and is also found in the skin, hair and nails. The claim that arsenic is or is not a normal constituent of living tissue for performing certain functions is a problem for future investigation.

Manganese

Manganese is present in all plants and animals and is an essential element in nutrition. Rats born from mothers on a low manganese diet have a high mortality rate and are usually not strong enough to survive birth. If they do survive, they are not active enough to suckle. It has been shown that manganese is necessary for reproduction. By reducing the manganese content of the

diet for rats, egg formation fails to occur and reproduction is therefore impossible.

It has been suggested that the function of manganese may be concerned with the development of the pituitary gland and regulation of the sex glands. When manganese is ingested, it is stored primarily in the liver, but under normal conditions it leaves the blood rapidly. The manganese requirements for man have not been determined. It has been suggested that the diet of children should contain between 0.2 and 0.3 mg. of manganese per kilogram of body weight per day.

Sources

The best food sources of manganese are:

Foods	*Milligrams Manganese per 100 grams of food*	*Remarks*
Blueberries	4.44	
Filberts	4.17	Amt. used to be considered
Chestnuts	3.67	Amt. used to be considered
Pecans	3.48	Amt. used to be considered
Black walnuts	3.20	Amt. used to be considered
Graham bread	3.16	1 slice 27-36 gm., ± 1.05
Dried peas	2.77	No figures available
Navy beans	2.54	On cooked, dried, vegetable
Ralston's cereal (100 gm. portion cooked)	1.82	20 gm., dry basis
Brown rice	1.70	
Barley, cooked	1.49	
Turnip greens	1.42	

OTHER MINERALS

Bromine

The metabolism of bromine is similar to that of chlorine but the two are not interchangeable. Bromine is found as a normal constituent of all tissues. As is the case with chlorine, bromine is excreted chiefly by the kidneys. (Blood serum contains about 1 mg. of bromine per 100 cc. while the cells only contain 0.5 mg. per 100 cc.)

Much interest has been aroused as to the role of bromine in animal life, since low blood bromine values were found in individuals who suffered from depressive psychoses. Some workers claimed that the pituitary gland has a bromine content fifteen to thirty times that found in the blood.

Bromine given in large amounts (ingested) causes stupor and skin eruptions; and like chlorine, when given in excess it may cause generalized edema. Acting as a general protoplasmic poison in animals and man, bromine causes redness and blistering of the skin, when applied to it in solution; and when swallowed, it arouses inflammation of the mouth, throat, and stomach. Bromine, like chlorine, may cause poisoning in industrial use.

Zinc

Zinc, like iron, is found in all tissues and foodstuffs. The total zinc content of the body is 2.2

grams, which is about one-half of the iron content of the adult. Under normal conditions about 15 to 20 mg. of zinc are eaten in our food. Zinc is excreted by the gastro-intestinal tract and by the kidneys. The liver and pancreas of various species of animals contain the largest amount of zinc while the lungs, brain and testicles contain but little. Many experiments indicate that zinc is an essential element in animal and plant nutrition.

When attempts were made to raise experimental animals on diets very low in zinc, it was found that the group of animals getting zinc lived 25 to 50 per cent longer than those on a diet containing little zinc. The growth of young rats fed a zinc-free diet was greatly inferior to that of animals that received a normal amount of zinc. It has been demonstrated that zinc is an essential element in the nutrition of the rat because of its growth-promoting properties.

The rate of absorption of carbohydrate and proteins from the gastro-intestinal tract is influenced by the concentration of zinc in the diet. In zinc-deficient rats, a distinct delay in the tissue-interval for absorption of both carbohydrate and protein from the gastro-intestinal tract has been proved. This delay in the rate of absorption

leads to a decrease in the efficiency of converting food into body tissues.

Another interesting observation concerning the possible action of zinc is its presence as a constituent of insulin crystals no matter how they are prepared. Zinc has been found to be present in the pancreas. It has also been found in all commercial preparations of insulin. But when more zinc is added to insulin solutions, the action of insulin is delayed by the presence of the zinc salt. The zinc content of the pancreas in a diabetic person is one-half that of the non-diabetic. It has been suggested that part of the zinc in the pancreas may be concerned with the storage and utilization of insulin.

Zinc is an essential and indispensable element in nutrition. There appears to be no danger of a deficiency of zinc in the average diet.

Copper

During the past few years the study of copper metabolism has stepped into the limelight along with that of iron and other elements which occur in extremely small quantities in the body. Copper occurs in all the tissues; the largest amounts are found in the liver, spleen and kidneys. Human blood contains 1.0 to 2.0 mg. of copper per quart of serum and human milk contains less than

one-half of this amount per quart. Cow's milk contains much less copper than human milk. That copper occurs in foodstuffs has, of course, been known for some time. No physiological function had been assigned to copper until 1928, when Hart, Steenbock, Waddell and Elvehjem proved that it is necessary as a supplement to iron for the formation of hemoglobin.

In infants as well as in experimental animals, a diet limited to milk causes the development of a nutritional anemia. It was believed that this anemia was wholly due to a deficiency of iron in milk, but the addition of inorganic iron salts to milk did not prevent anemia. Animals fed on a milk diet, with or without added iron, became weak; growth ceased, and death followed. When small amounts of copper salts were added to the diet, a very different course ensued. The animals became alert, the blood count and hemoglobin increased, and recovery followed. The addition of a "trace mineral" was the determining factor between life and death! Many investigations in the field of nutrition have shown that cow's milk (whole) is inadequate for normal maintenance of experimental animals. The addition of copper and iron to an exclusive milk diet protects against nutritional anemia and produces an apparent well-being in animals as judged by hemoglobin

formation, growth and reproduction. In the nutritional anemia of suckling pigs, iron alone stimulates hemoglobin synthesis as well as does iron supplemented with copper. This has led to the opinion that pigs had some undetected available source of copper, or that in pigs an iron deficiency occurs before there is any copper deficiency. The anemia which is common among yearlings and heifer's suckling calves responds rapidly to iron salts fortified with copper sulfate. Iron supplements alone have proved inadequate in curing this condition.

The new-born calf has a store of copper in its liver about eight times as large as is found in the adult animal's liver. The amount of copper in the body of a new-born rat is nearly double that in an adult rat. Analyses of infant cadavers have revealed that smaller amounts of copper are found in the livers of anemic infants than in non-anemic infants. These points of resemblance in the storage of iron and copper suggest that nutritional anemia may be due in part to a copper deficiency. The evidence suggests that copper does play some part in hemoglobin synthesis.

When to one group of anemic infants, iron and copper are given, and only iron to another, it was found that a more rapid recovery occurred in the group that received both iron and copper.

For a maximum rise in hemoglobin some factor was needed in addition to iron; this factor is not sufficiently supplied by food but is supplied by copper. The efficacy of copper as a prophylactic agent against the anemia of infancy was observed among foundlings. The children that received copper and iron had hemoglobin values 19 per cent above those that did not receive these mineral elements.

Copper does not form part of the hemoglobin molecule and does not combine with iron directly in forming hemoglobin. The action of copper appears to be that of promoting reactions in which it does not itself take part. Perhaps by liberating more iron from the liver for use by the bone marrow, or by converting iron which is stored into a chemical form more suitable for inclusion in the hemoglobin molecule, copper exerts this promoting function. Most workers are agreed that copper is necessary as a supplement to iron for hemoglobin formation. It has been established that copper is not concerned with iron assimilation but functions in converting the absorbed iron into hemoglobin.

Sources

The best food sources of copper are:

Foods	*Milligrams Copper per 100 grams of food*
Calves' liver	4.41
Oysters	3.07
Beef liver	2.15
Sweet chocolate	2.00
Mushrooms	1.79
Nuts	.96-1.36

Cobalt and Nickel

The importance of cobalt in nutrition has taken on increased significance from recent work in Australia and New Zealand which has demonstrated its value in the treatment of certain fatal diseases of sheep and cattle. A type of nutritional anemia which is generally called "Pine disease" occurs both in sheep and cattle. The symptoms include progressive emaciation, loss of appetite, and pallor of the visible membranes. Usually there occurs a reduction in the red cell count and also in the hemoglobin values. Many workers report that treatment with doses of cobalt salts results in marked improvement in weight, appetite and in the anemia.

The nutritional anemia of cud-chewing animals was formerly dealt with by giving them iron compounds. The presence of cobalt has been demonstrated in all substances which have proved of value in combating the disease. Nickel,

even in traces, increased the action of cobalt salts. The anemia can be cured, and even prevented, by giving cobalt salts without iron. The quantity of cobalt required to cure affected sheep is 1 mg. daily for a period of two weeks. This work suggests that cobalt must be regarded as an essential element in nutrition. The presence of traces of cobalt may have a more significant effect than has been recognized.

When nickel and cobalt are ingested, they are excreted chiefly by the gastro-intestinal tract. The production of red cells in excess of the normal is caused by addition of cobalt to the diet in animals. Both nickel and cobalt occur in extremely small amounts in living tissues; and they have not received sufficient attention in human nutritional studies. A place for cobalt may yet be found in the treatment of nutritional anemia in man.

Selenium

Recent investigations reveal the fact that plants in certain regions contain selenium in concentrations that are sufficient to produce poisonous effects in animals. The disturbances in livestock referred to as "alkali disease" and "blind staggers" have been shown to be due to the selenium present in the vegetation. Any soil that contains

0.5 part per million or more of this element may be regarded as dangerous.

Plants vary widely in their ability to take up selenium from the soil. Those plants which absorb large quantities of sulfur were found to contain large amounts of selenium also. The addition of sulfur to selenium-bearing soil decreases the damage to the plant as well as the amount of selenium absorbed.

Loss of hair from the mane and tail of horses and a general loss of hair from swine are the most obvious symptoms of this toxic agent upon these species of domestic animals. Abnormal hoof development, together with a sloughing off of the old hoofs, is a common occurrence. Eggs from affected farms show extremely low hatchability. Growth of chicks is inhibited. Selenium however does not present a great menace to the public health.

Fluorine

Many investigators have held the view that fluorine is an essential element in animal metabolism. It is universally distributed in the tissues and is especially high in bones, teeth and skin. Fluorine is found in all foods. That fluorine in too high concentration in the diet can have a poisonous effect has been demonstrated in cattle.

Other farm animals, such as swine and chickens, are likewise subject to fluorine intoxication. Sea water contains much fluorine, and it is also present in sea fish.

When the fluorine intake of the cow is increased, an increased fluorine output in the cow's milk is not found. When the intake of fluorine in the hen is increased, the fluorine content of the yolk of the egg is markedly increased. This suggests that fluorine is in the egg in combination with the fatty substances of the yolk.

Attempts have been made to remove fluorine from drinking water, in which it is a danger to public health, and is one cause of mottled teeth. In the course of chronic poisoning the fluorine accumulates in the tissues, in the bones and in the teeth. It is generally believed that amounts of fluorine in drinking water greater than 1 to 2 mgs. per liter will cause mottled teeth. Recently amounts in excess of these figures were found to be excreted by normal individuals.

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Chapter 12

Pregnancy

Pregnancy, under normal conditions, is a physiologic process. However, it does make special demands on the maternal organism and diets that are adequate under ordinary circumstances fail to meet the increased requirements for mineral elements. The pregnant woman is subject to the nutritional requirements for fetal growth, for the preparation of her own body tissues for parturition, and for the future production of milk. Protein, fat and carbohydrate foodstuffs furnish the necessary sources of energy for the body, and protein supplies the material for building up new tissue. But these three foodstuffs fail to supply all the materials necessary for the maintenance of life.

Mineral elements in addition to the foodstuffs are essential. All cells, tissues and fluids of the body contain mineral salts which supply the necessary balance of ions for the normal functioning of cells. *Without mineral elements no new body tissue can be formed.* It has been estimated that for each gram of protein laid down in the

body, about 0.3 gram of mineral matter is stored. The growing fetus requires a liberal supply of all minerals during the entire pregnancy, and a particularly large supply during the last two months.

Animals placed on deficient mineral diets during pregnancy suffer from a marked loss of calcium and phosphorus from the body. The pregnant woman has an added demand for calcium and phosphorus, but has no added storage space available for mineral elements. The pregnant woman, even on a low calcium diet, was found to excrete the usual normal amount of calcium. This observation of Bauer and his co-workers shows that the demand for calcium by the growing fetus does not decrease the amount of calcium required for excretion. When the calcium intake is insufficient to provide adequately both for excretion and for the growth of the fetus, the requirements of the fetus are fulfilled at the expense of the mother's stores of calcium.

At the end of the sixth month of pregnancy the fetus contains about five grams of calcium, and at birth the baby's body contains thirty grams of this mineral. It is evident that during the last twelve weeks of pregnancy, the fetus increased its calcium content by twenty-five grams. This means that about two grams of cal-

cium per week were demanded by the fetus from the mother during the last twelve weeks of pregnancy. If the pregnant woman does not get more than this amount, she withdraws the calcium requirements for the baby from the accumulated storage depots in her own bones.

Modern x-ray equipment enables one to see not merely the outline of the bones but also their architecture. Todd and his co-workers even ascertained the fluctuation of the mineral content in the bones during pregnancy by taking x-rays of the mother's hands and feet, the places in which this fluctuation is most easily demonstrated. Even after the baby was born the mother's bones continued to show a drain on the calcium reserve. This is because the calcium is now going into the milk. If the mother does not nurse her baby she still depletes the calcium stores in her bones. Although she is not actually producing milk, she is still freeing the milk constituents in her body, and those that are not utilized are eliminated from the system by the excretory pathways.

That marked differences in the degree of hardening (calcification) of fetal skeletons exist has recently been shown by Dieckmann and his co-workers. An increase of twenty per cent in the calcium and phosphorus content was found

in a seven-month old fetus whose mother had been on a controlled mineral intake. It appears that probably all cases of fetal rickets are due to mineral-deficient diets during pregnancy. The maternal organism mobilizes calcium from the so-called depots, or storage-points, until softening of the bones results; even then fetal rickets cannot be prevented. By means of x-ray examinations of bones of normal infants, Coons and Blunt concluded that the calcification of the bones was best where the mother's retention of calcium and phosphorus during pregnancy was highest. The mothers of infants with soft skulls had diets grossly deficient in calcium. Toverud found that the extent of hardening of fetal skulls depended upon the calcium content of the maternal diet.

The calcium and phosphorus requirements of the mother during pregnancy are satisfied by a diet that produces an excess of these minerals. Most workers have found that the requirements sufficient to produce an excess of calcium during pregnancy vary from 1.4 to 1.8 grams of calcium daily. The phosphorus requirements have been found to be satisfied on intakes from 1.4 to 2.0 grams of phosphorus daily.

Milk and leafy vegetables are foods rich in calcium, and apparently among the best sources of

calcium and phosphorus are milk and cheese. One quart of milk contains 1.2 grams of calcium and 0.9 gram of phosphorus. It is evident that at least one quart of milk daily is necessary to bring the calcium intake to the required level. The calcium content of one quart of milk is found in five ounces of cheese or one dozen oranges. Calcium salts are more expensive than milk and are usually excreted almost quantitatively in the urine and feces. It has been estimated that it would require 8 grams of dicalcium phosphate to equal the amount obtained from one quart of milk.

Magnesium

It has been found that a daily intake of 0.35 to 0.45 gram of magnesium was sufficient to give the required excess in the latter part of pregnancy. When foods that contain sufficient calcium and phosphorus are ingested during pregnancy, the magnesium requirement is also satisfied.

Iron

That depletion of the mother's stores of iron occurs with successive births is known. The child's hemoglobin values are normal at birth even when the mother's hemoglobin was found

to be low during the pregnancy. Coons found that the average maternal intake of 15 mg. of iron a day permitted an average retention of 3.2 mg. This amount is sufficient to provide for the needs of both mother and fetus. Other workers, Macy and Hunscher, found that 20 mg. of iron daily was desirable during pregnancy. The foods rich in iron are liver, kidney, gizzards, red meats, raisins, prunes, apricots and peaches.

Iodine

Where goiter is due to local conditions, such as lack of sea salt, which contains iodine, the iodine content of the diet must be considered. The amount of iodine needed during pregnancy may be supplied by the use of iodized salt and sea foods.

Copper

Copper deficiency may occur, but it is infrequent. During pregnancy the copper content of the blood has been found to be increased. For a maximum rise in hemoglobin some factor is needed in addition to iron; this factor is not sufficiently supplied by food, but is supplied by copper. Copper does not form part of the hemoglobin molecule and does not combine with iron directly in forming hemoglobin.

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Chapter 13

Lactation

A lactating mother requires minerals both for the maintenance of her own tissues and for secretion in the milk. These mineral elements can be derived either from her food intake or from her own mineral reserves. The occurrence of bone-softening (osteomalacia) in cows, goats, rats, and woman after repeated pregnancies demonstrates that calcium must be withdrawn from the maternal organism under such conditions. The mineral concentration of mother's milk tends to remain fairly constant, and the total quantity of minerals excreted in milk depends upon the volume of milk produced.

The intake of energy foodstuffs and mineral elements necessary for the production of milk in the lactating mother is materially increased over that in pregnancy. Many studies on the caloric requirements of the lactating woman show that 40 to 50 per cent of the total caloric intake reappears in the mother's milk. A good source of supply of mineral elements for the lactating mother is a mixed diet containing at least

one quart of milk daily. At the height of lactation, even on the above diet, it is difficult to procure a sufficient excess of calcium. It has been estimated that the daily calcium intake must be four times that present in the secreted milk to prevent or retard loss of calcium from the mother's stores during lactation. The daily calcium intake during this period should amount to 2 grams of calcium or more, preferably from milk. Even one year after cessation of lactation, calcium deficiencies have been found. The better the storage of calcium and phosphorus during pregnancy, the greater the reserve for lactation.

Milk and the Infant

The nutrition of the infant must provide for the high energy requirements and for normal growth and development. The metabolic processes of the infant are much more active than those of the adult. To supply this material for growth and to allow for a high energy exchange, the infant requires a large intake of food per unit of body weight. The protein need of the infant is greater than that of the adult because of the rapid growth. As a readily available source of energy for the body, the infant needs more carbohydrate per unit of weight than the adult.

The fat in both human and cow's milk provides approximately one-half of its caloric value.

No new body tissue can be formed without mineral elements. When the infant's diet is deficient in any of the essential minerals, normal growth and function cease. A constant excretion of minerals occurs even on a mineral-free diet. Unless at least an equivalent amount of minerals is added to the diet, wasting of the body occurs. About 0.3 gram of mineral elements is also stored for each gram of protein laid down in the infant's body.

Milk is the principal food of the infant and contains a rich supply of mineral elements. Besides containing large amounts of calcium, milk contains all the minerals which are essential for life. However, *the amount of iron present is insufficient when milk is the only source of iron fed the infant.*

Sodium

When an infant receives a sufficient supply of human milk to meet his energy and growth requirements, it has been found that an adequate amount of sodium salts is also present. The sodium content of cow's milk is three times the quantity found in mother's milk. Hence, an

infant receiving artificial feedings usually receives an adequate amount of this mineral.

Sodium chloride (salt) occurs in the extracellular fluids of the body, the blood plasma, lymph, cerebrospinal fluid and in the gastro-intestinal secretions. A constant supply of sodium salts in the diet is essential because there is a loss of these salts at all times by way of the urine, sweat and the gastro-intestinal secretions. When diarrhea is present, large amounts of sodium chloride are lost by way of the bowel.

Potassium

When new body tissues are built, as in infancy, the potassium requirements are at the maximum. Human milk and cow's milk contain an excess of potassium over sodium salts. There is sufficient potassium in either milk to meet the nutritional demand for this mineral.

Potassium salts are present within all the cells of the tissues, and in the red blood cells; but only small amounts are present in the body fluids. The potassium requirements of the infant are greater than that of the adult.

Calcium

Cow's milk contains about three to four times as much calcium as human milk. There is suf-

ficient calcium in both milks to meet the needs of the average infant if sufficient amounts are ingested. The infant requires relatively large amounts of calcium for bone growth and for the maintenance of the calcium content of the blood plasma. Symptoms of tetany may occur unless the calcium content of the blood plasma are above a definite minimum level. The amount of calcium absorbed and retained is influenced largely by the amount of vitamin D in the diet.

Magnesium

The amount of magnesium needed by the infant is not definitely known. However, human milk appears to contain a sufficient supply to meet the requirements. Cow's milk contains twice as much magnesium as human milk. Magnesium is present in the bones, muscles, and blood serum.

Iron

Breast milk contains about 0.5 mg. of iron per quart and cow's milk 0.2 mg. The iron requirement of the infant is 1 to 2 mg. per day; and hence *it is impossible to meet this demand from milk alone.*

Copper

Raw cow's milk has been found to contain less copper than human milk. Pasteurization of cow's milk in receptacles of copper and alloys of copper results in an increase in the copper content of milk.

Iodine

Sufficient amounts of iodine are present in human and cow's milk to meet the needs of the infant. In goitrous regions both human and cow's milk may be deficient in iodine.

Chlorides

The normal chloride requirements of the infant are adequately supplied by both human milk and cow's milk. The addition of sodium chloride (salt) to the diet is unnecessary.

Phosphates

Human milk contains all the phosphate that is required and cow's milk contains at least seven times the amount required by the infant. The excess phosphate in cow's milk makes for poorer calcium absorption.

Sulfur

The protein content of both human and cow's

milk supplies the sulfur need of the infant adequately.

Water

Because of the more active metabolism of the infant, the water requirement in proportion to body weight is higher than in the adult. The average normal breast-fed infant under one year of age receives enough water from milk alone to meet most of the needs. If too little water is taken in, there will not be a normal gain in weight. With artificial feedings, the protein and salt content of the diet are higher than with human milk. Hence, for the elimination of the added salt and protein waste products more water is required than when breast milk is fed. With a salt-deficient diet, starvation, and prolonged diarrhea, the body is incapable of maintaining a normal water content.

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Chapter 14

Summary

The minerals have specific and varied functions in the human economy. The performance of these vital functions depends upon the ingestion, utilization and excretion of these mineral elements. *The amount of minerals contained in natural foodstuffs* is the prime factor in determining the amount ingested. A great deal of emphasis has been placed on the importance of providing an adequate amount of minerals in the diet through proper selection of food. Formerly, it was held that organic iron was essential for hemoglobin formation.

In a masterly review of the subject, Shohl * states that cereals and carbohydrates furnish nearly one-half of the fuel value and only one-sixth of the mineral content of the daily average human diet. Milk, which provides only one-sixth of the calories, accounts for nearly half of the mineral supply.

* A. T. Shohl, "Mineral Metabolism," Reinhold Publishing Corp., 1939.

SUMMARY

Sodium Chloride

Life cannot be supported and normal growth cannot take place when the sodium intake is too low. No human diet, even without added salt, is so low in sodium content that it cannot support life. The amount of sodium chloride consumed in the United States per person has been estimated at about 10 grams daily. When 35 to 40 grams of sodium chloride are ingested by a normal person, swelling of the body occurs. When vegetable intakes are high, sodium chloride is particularly desired. The liberal use of salt facilitates the formation of gastric juice and permits a freer flow of saliva and other intestinal secretions.

Sodium chloride is the most abundant electrolyte in the blood and intercellular body fluid. It is in the medium of sodium ion and chlorine ion that the enzymatic actions of digestion take place.

Potassium

The potassium requirements for normal growth and maintenance have been found to be amply supplied by the potassium content of a diet that is adequate in other respects. Potassium intake is of no practical concern because the potassium content of the diet, 2-3 grams per day, is ample to meet the body's need for this mineral.

The body contains more potassium than sodium, and during periods of growth this difference is even more marked. In rapid growth it is desirable to supply the body with an excess of potassium over sodium in the food intake. In adults the potassium requirements are at the minimum. The potassium in the cell is associated with phosphorus, and not all the potassium is found in the ionized state.

Calcium

Calcium is present in the body in a larger amount than any other mineral element. The skeleton is the normal storage point of calcium, and very little is present in other tissues. However, that small fraction of calcium that is not present in the skeleton is of importance in determining the state of health of the body. Although a normal amount of calcium may be ingested, this does not insure that it will be assimilated and used. Frequently, a large proportion of the calcium occurs in the diet in insoluble form, and assimilation by the gastro-intestinal tract is impossible. It has been estimated that the adult diet should contain 1 gram of calcium for every 100 grams of protein in the diet.

It has been shown that the presence of certain mineral salts of sodium, potassium and calcium

in balanced proportions are necessary for vital action. Sodium ions and potassium ions decrease muscle irritability. Calcium appears to be concerned in the transformation of chemical energy into muscular contractions, and the importance of calcium to normal hardening (calcification) of bones is obvious.

Magnesium

Magnesium and calcium are both stored in the bones, but magnesium is present in the body cells in a far greater concentration than is calcium. The chief source of magnesium in the average diet is *vegetables*. An adequate amount of magnesium is present in the human dietary and the average intake of 0.27 gram per day appears to be adequate. Deprivation of magnesium causes overexcitability, and is followed by the development of malnutrition and marked reduction in growth. Solutions that are low in magnesium ions appear to favor bone hardening. The effects of magnesium ions are usually antagonistic to those of the calcium ions. Magnesium is present in large amounts in the red cells in the form of magnesium ions.

Phosphorus

When there is even a slight lack of phosphorus

in the diet, normal growth is prevented. The minimum requirements for the adult average about 0.68 gram of phosphorus per day merely to replace the loss of this mineral from the body. Only a few of the American dietaries fall below this level. The forms of phosphorus ingested depend upon the type of food. Milk contains the protein, casein, which is relatively high in phosphorus. Although our knowledge of the chemical reactions which occur during muscular contraction and recovery is not complete, *phosphorus compounds are essential for normal muscle activity.*

The phosphorus present in the skeleton in the form of tricalcium phosphate is the largest deposit of phosphorus in the body. Phosphorus is essential for vital activity and particularly for *cell division.* The inorganic phosphates are found to be completely ionized in the blood serum.

Sulfur

Unlike phosphorus, organic sulfur compounds are essential for the maintenance of life, and every cell in the body contains sulfur. Sulfur-containing amino acids are needed for growth. When an individual is on a diet in which the protein intake is adequate, sulfur intake is not a nutritional problem. The recognition of the amino

acid *methionine* as an "essential" protein unit has resulted in a renewed study of sulfur compounds.

Iron

Although the amount of iron present in man is small, it is vital in the living processes concerned with the transport of oxygen and with the metabolism of food materials within the cells. Various workers have estimated that the amounts of iron necessary for meeting the requirements of maintenance in the adult are from 5 to 15 mg. per day. Small quantities of iron are supplied by everything that we eat, but no single food contains enough iron to provide adequate intake in a single portion. It has been proved that inorganic iron is absorbable and is of value in nutrition, and that organic compounds are of little value.

Iodine

The daily amounts of iodine required for the prevention of goiter obviously vary in different localities, ages, climate and diets. The normal requirements of the body for iodine are not yet known. It has been estimated that 0.04 to 0.08 mg. of iodine would suffice for the normal daily needs of an adult. Iodine is effective in the prevention of goiter when taken in any form. The

utilization of iodine to form thyroid hormone is an integral part of thyroid activity.

Zinc

Zinc, like iron, is found in all tissues and foodstuffs. It is an essential and indispensable element in nutrition. On the average diet there appears to be no danger of a deficiency of this element.

Copper

Copper is necessary as a supplement to iron for hemoglobin formation. The additions of copper and iron to an exclusive milk diet protect against nutritional anemia. For a maximum rise in hemoglobin, some factor is needed in addition to iron. This factor is not sufficiently supplied by food, but is supplied by copper, which appears to act as a promoter of the reaction which converts absorbed iron into hemoglobin.

When the mineral content of our foodstuffs is inadequate, the amounts needed can be taken in the form of inorganic mineral salts. Sulfur is the only mineral element which must be supplied in organic form. This element is furnished by the proteins of the diet.

SUMMARY

The total mineral content of a diet cannot serve as an index for the adequacy of the mineral supply since such an index ignores the specific role of each mineral. One mineral cannot be substituted for another. The separate and distinct functions of the various minerals maintain, in the human economy, the normal and proper performance of the vital functions in our bodies. The performance of these vital functions is dependent upon the ingestion, utilization and excretion of these mineral elements.

INDEX

INDEX